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(54) **Title: PIPERAZINE DERIVATIVES AND PROCESS FOR THE PREPARATION THEREOF**

(54) **Titre: DERIVES DE PIPERAZINE ET LEUR PROCEDE DE PREPARATIONON THEREOF**

(57) Abstract

The present invention relates to a novel compound of general formula (I) and its pharmaceutically acceptable acid addition salt, and process for the preparation thereof, which have strong antitumor activities and very low toxicity, wherein R¿1 and R¿2 are independently hydrogen, C¿1-C¿4 alkyl, C¿1-C¿4 alkylcarboxyl, C¿1-C¿4 alkylcarbonyl, C¿1-C¿4 alkoxy, C¿1-C¿4 hydroxyalkyl, C¿1-C¿4 aminoalkyl or C¿1-C¿4 hydroxyiminoalkyl, or R¿1 and R¿2 are fused to form C¿3-C¿4 unsaturated ring; R¿3, R¿4, R¿5, R¿6 and R¿7 are independently hydrogen, halogen, hydroxy, nitro, amino, C¿1-C¿4 alkyl, C¿1-C¿4 alkylcarboxyl, C¿1-C¿4 alkylcarbonyl, C¿1-C¿4 alkoxy or C¿1-C¿4 thioalkoxy; R¿8 is C¿1-C¿4 alkyl; Y is oxygen, sulphur, amino, substituted amino or C¿1-C¿4 thioalkyl; Z is C¿1-C¿4 alkoxy, C¿1-C¿4 alkyl, C¿1-C¿4 alkylamino or C¿1-C¿4 thioalkoxy; X¿1 and X¿2 are independently carbon or nitrogen; and -N--C- and -C--Y- may form a single bond or a double bond provided that if -N--C- forms a single bond, -C--Y- forms a double bond, and if -C--Y- forms a single bond, -N--C- forms a double bond and R¿8 is nonexistent.

(57) Abrégé

L'invention concerne un nouveau composé de formule générale (I) et son sel d'addition acide pharmaceutiquement acceptable ainsi que son procédé de préparation présentant des activités anticancéreuses marquées et une très faible toxicité, dans laquelle R¿1 et R¿2 représentent indépendamment un hydrogène, C¿1-C¿4 alkyle, C¿1-C¿4 alkylcarboxyle, C¿1-C¿4 alkylcarbonyle, C¿1-C¿4 alcoxy, C¿1-C¿4 hydroxyalkyle, C¿1-C¿4 aminoalkyle ou C¿1-C¿4 hydroxyiminoalkyle, ou R¿1 et R¿2 sont fusionnés pour former un noyau insaturé C¿3-C¿4; R¿3, R¿4, R¿5, R¿6 et R¿7 représentent pris séparément un hydrogène, halogène, hydroxy, nitro, amino, C¿1-C¿4 alkyle, C¿1-C¿4 alkylcarboxyle, C¿1-C¿4 alkylcarbonyle, C¿1-C¿4 alcoxy ou C¿1-C¿4 thioalkoxy; R¿8 représente C¿1-C¿4 alkyle; Y représente un oxygène, soufre, amino, amino substitué ou C¿1-C¿4 thioalkyle; Z représente C¿1-C¿4 alcoxy, C¿1-C¿4 alkyle, C¿1-C¿4 alkylamino ou C¿1-C¿4 thioalkoxy; X¿1 et X¿2 représentent pris séparément un carbone ou azote; et -N--C- et -C--Y- peuvent former une seule liaison ou une double liaison à condition que, lorsque -N--C- forme une seule liaison, -C--Y- forme une double liaison, et que lorsque -C--Y-, -N--C- forme une double liaison et que R¿8 ne soit pas présent.

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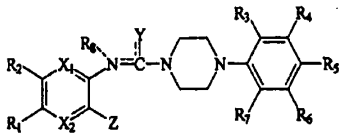

(I)

(57) Abstract

The present invention relates to a novel compound of general formula (I) and its pharmaceutically acceptable acid addition salt, and process for the preparation thereof, which have strong antitumor activities and very low toxicity, wherein R_1 and R_2 are independently hydrogen, C_1–C_4 alkyl, C_1–C_4 alkylcarboxyl, C_1–C_4 alkylcarbonyl, C_1–C_4 alkoxy, C_1–C_4 hydroxyalkyl, C_1–C_4 aminoalkyl or C_1–C_4 hydroxyiminoalkyl, or R_1 and R_2 are fused to form C_3–C_4 unsaturated ring; R_3, R_4, R_5, R_6 and R_7 are independently hydrogen, halogen, hydroxy, nitro, amino, C_1–C_4 alkyl, C_1–C_4 alkylcarboxyl, C_1–C_4 alkylcarbonyl, C_1–C_4 alkoxy or C_1–C_4 thioalkoxy; R_8 is C_1–C_4 alkyl; Y is oxygen, sulphur, amino, substituted amino or C_1–C_4 thioalkyl; Z is C_1–C_4 alkoxy, C_1–C_4 alkyl, C_1–C_4 alkylamino or C_1–C_4 thioalkoxy; X_1 and X_2 are independently carbon or nitrogen; and –N=C– and –C=Y– may form a single bond or a double bond provided that if –N=C– forms a single bond, –C=Y– forms a double bond, and if –C=Y– forms a single bond, –N=C– forms a double bond and R_8 is nonexistent.

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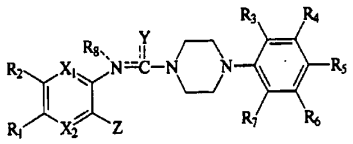
Description

Piperazine derivatives and process for the preparation thereof

The present invention relates to a new piperazine derivative of the general formula (I) or its pharmaceutically acceptable acid addition salt, and process for the preparation thereof.



(I)

wherein R_1 and R_2 are independently hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylcarboxyl, C_1-C_4 alkylcarbonyl, C_1-C_4 alkoxy, C_1-C_4 hydroxyalkyl, C_1-C_4 aminoalkyl or C_1-C_4 hydroxyiminoalkyl, or R_1 and R_2 are fused to form C_3-C_4 unsaturated ring;

R_3, R_4, R_5, R_6 and R_7 are independently hydrogen, halogen, hydroxy, nitro, amino, C_1-C_4 alkyl, C_1-C_4 alkylcarboxyl, C_1-C_4 alkylcarbonyl, C_1-C_4 alkoxy or C_1-C_4 thioalkoxy;

R_8 is C_1-C_4 alkyl;

Y is oxygen, sulphur, amino, substituted amino or C_1-C_4 thioalkyl;

Z is C_1-C_4 alkoxy, C_1-C_4 alkyl, C_1-C_4 alkylamino or C_1-C_4 thioalkoxy;

X_1 and X_2 are independently carbon or nitrogen; and

—N=C— and —C=Y— may form a single bond or a double bond provided that if —N=C— forms a single bond, —C=Y— forms a bouble bond, and if —C=Y— forms a single bond, —N=C— forms a bouble bond and R_8 is nonexistent.

In the above definitions, C_1-C_4 alkyl means methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl or tert-butyl.

C_1-C_4 alkylcarboxyl means carboxyl esterified with a lower alkyl such

as methylcarboxyl and ethylcarboxyl.

C_1-C_4 alkylcarbonyl means carbonyl ketonized with a lower alkyl such as methylcarbonyl and ethylcarbonyl.

C_1-C_4 alkoxy means methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy or tert-butoxy.

C_1-C_4 thioalkoxy means methylthio, ethylthio, propylthio, isopropylthio, butylthio, isobutylthio or tert-butylthio.

C_1-C_4 aminoalkyl means aminomethyl, aminoethyl, aminopropyl, aminobutyl or the like.

C_1-C_4 kydroxyalkyl means hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl or the like.

C_1-C_4 hydroxyiminoalkyl means C_1-C_4 alkyl substituted with hydroxyimino such as hydroxyiminoethyl.

Substituted amino means hydroxyamino, C_1-C_4 alkylamino, C_1-C_4 alkoxyamino or the like.

The present inventors had studied for a long time to find compounds having intensive antitumor activity. As a result, now we have finally found out the facts that the present compounds of the general formula (I) and acid addition salts thereof have not only prominent antitumor activities but very low toxicities.

Accordingly, the one object of the present invention is to provide the novel compounds of the general formula (I) and acid addition salts thereof having not only prominent antitumor activities but very low toxicities.

The other object of the present invention is to provide a process for the preparation of the compounds of general formula(I) and acid addition salts thereof.

The compounds of the present invention can be mixed with pharmaceutically acceptable vehicles by a known method to give pharmaceutical compositions and thus the pharmaceutical compositions

can be used to prevent or treat with various kinds of tumors of human beings or mammals.

Therefore, another object of the present invention is to provide pharmaceutical compositions containing the compound of the general formula(I) or an acid addition salt thereof as an active ingredient.

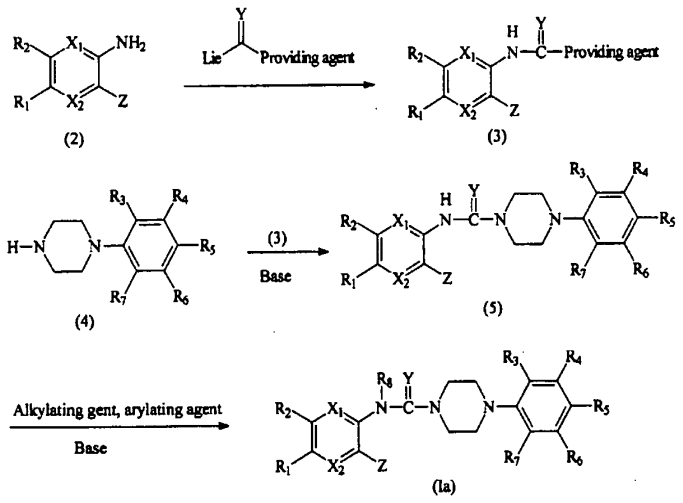
Acids which can be reacted with the compounds of the general formula(I) to form acid addition salts are pharmaceutically acceptable inorganic or organic acids; for example, inorganic acids such as hydrochloric acid, bromic acid, sulfuric acid, phosphoric acid, nitric acid; organic acids such as formic acid, acetic acid, propionic acid, succinic acid, citric acid, maleic acid, malonic acid, glycolic acid, lactic acid; amino acids such as glycine, alanine, valine, leucine, isoleucine, serine, cysteine, cystine, asparaginic acid, glutamic acid, lysine, arginine, tyrosine, proline; sulfonic acids such as methane sulfonic acid, ethane sulfonic acid, benzene sulfonic acid, toluene sulfonic acid; or the like.

Vehicles which can be used in the preparation of pharmaceutical compositions containing the compound of the general formula (I) as the active ingredient may include a sweetening agent, binding agent, dissolving agent, aids for dissolution, wetting agent, emulsifying agent, isotonic agent, adsorbent, degrading agent, antioxident, antiseptics, lubricating agent, filler, perfume or the like; such as lactose, dextrose, sucrose, mannitol, sorbitol, cellulose, glycine, silica, talc, stearic acid, stearin, magnesium stearate, calcium stearate, magnesium aluminum silicate, starch, gelatine, tragacanth gum, glycine, silica, alginic acid, sodium alginate, methyl cellulose, sodium carboxy methyl cellulose, agar, water, ethanol, polyethylenglycol, polyvinyl pyrrolidone, sodium chloride, potassium chloride, orange essence, strawberry essence, vanila aroma or the like.

Daily dosage of the compound of the general formula (I) may be varied depending on age, sex of a patient, degree of disease, etc. and generally 1.0mg to 5,000mg per day may be administered one to several times.

The compounds of the general formula (I) according to the present invention wherein —N=C— forms a single bond and —C=Y— forms a bouble bond, may be prepared by the following scheme I.

Scheme I



wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, X_1, X_2, Y and Z are as defined above, and Lie is a conventional leaving group such as halogen, sulfonyl or the like.

The above process comprises reacting a compound of the general

formula (2) with a -C(=Y)- group-providing agent in an organic solvent to obtain a compound of the general formula (3) and successively reacting the compound of the formula (3) with a compound of the general formula (4) to give the compound of the general formula (5). Then, the compound of the formula (5) may be reacted with an alkylating agent or an arylating agent in the presence of a base to give a compound of the general formula (Ia).

The -C(=X)-group-providing agent used in the above reaction may include 1,1-carbonyldiimidazole, 1,1-carbonylthiodiimidazole, phosgene, thiophosgene, carbonyldiphenoxide and phenylchloroformate, and it may be used in an amount of 1 - 1.5 equivalent, preferably 1-1.1 equivalent to the starting compound.

The reaction may be carried out in a conventional organic solvent such as, for example, tetrahydrofuran, dichloromethane, acetonitrile, chloroform and dimethylformamide.

And also the reaction is preferably carried out in the presence of a coupling agent such as a conventional inorganic or an organic base. Such conventional inorganic or organic bases used in the reaction may include sodium hydride, potassium hydride, sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, sodium bicarbonate, potassium bicarbonate, triethylamine, pyridine and DBU.

The reaction may be carried out at a temperature between 3℃ and boiling point of the solvent used, preferably at 50℃-100℃ and for 5 - 48 hours, preferably for 10 - 24 hours.

The reaction of the compound (3) with the compound (4) to give the compound (5) may be carried out in the presence of a conventional organic solvent at the temperature of 50-100℃ for 5-48 hours. The compound (4) may be used by 1-1.5 equivalent.

And also the reaction is preferably carried out in the presence of a conventional inorganic or organic base, such as sodium hydride, potassium hydride, sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, sodium bicarbonate, potassium bicarbonate, triethylamine, pyridine, DBU or the like.

Then, the compound of the formula (5) may be reacted with an alkylating agent or an arylating agent in the presence of a conventional organic or inorganic base to give a compound of the general formula (Ia).

The alkylating agent and arylating agent used in the above step may include C_1-C_8 alkylhalide, C_1-C_8 alkylsulfonate, substituted or unsubstituted C_3-C_8 cycloalkyl halide, arylhalide, and substituted or unsubstituted C_3-C_8 cycloalkyl sulfonate.

C_1-C_8 alkyl halide means methyl chloride, methyl bromide, methyl iodide, ethyl chloride, ethyl bromide, ethyl iodide, propyl chloride, propyl bromide, propyl iodide, butyl chloride, butyl bromide, butyl iodide, pentyl chloride, pentyl bromide, pentyl iodide, bromo ehtylacetate or the like.

C_1-C_8 alkylsulfonate means methyl sulfonate, ethyl sulfonate, propyl sulfonate, butyl sulfonate, pentyl sulfonate or the like.

Substituted or unsubstituted C_3-C_8 cycloalkyl halides mean cyclopropyl chloride, cyclopropyl bromide, cyclopropyl iodide, cyclobutyl chloride, cyclobutyl bromide, cyclobutyl iodide, cyclopentyl chloride, cyclopentyl bromide, cyclopentyl iodide, cyclohexyl chloride, cyclohexyl bromide, cyclohexyl iodide, cyclopropyl methyl chloride, cyclopropyl methyl bromide, cyclopropyl methyl iodide, cyclobutyl methyl chloride, cyclobutyl methyl bromide, cyclobutyl methyl iodide, cyclopentyl methyl chloride, cyclopentyl methyl bromide, cyclopentyl methyl iodide, cyclohexyl methyl chloride, cyclohexyl methyl bromide, cyclohexyl methyl iodide, or the like.

Aryl halides may include benzyl chloride, benzyl bromide, benzyl iodide, benzoyl chloride, benzoyl bromide, benzoyl iodide, toluyl chloride,

toluyl bromide and toluyl iodide.

Substituted or unsubstituted C_3-C_8 cycloalkyl sulfonate may include cyclopropyl sulfonate, cyclobutyl sulfonate, cyclopentyl sulfonate, cyclohexyl sulfonate, cyclopropyl methyl sulfonate, cyclobutyl methyl sulfonate, cyclopentyl methyl sulfonate and cyclohexyl methyl sulfonate.

Aryl sulfonate may include benzyl sulfonate, benzoyl sulfonate, toluyl sulfonate, or the like.

The reaction may be carried out in a conventional organic solvent as such as, for example, tetrahydrofuran, dichloromethane, chloroform, dimethyl sulfoxide, acetonitrile and dimethylformamide.

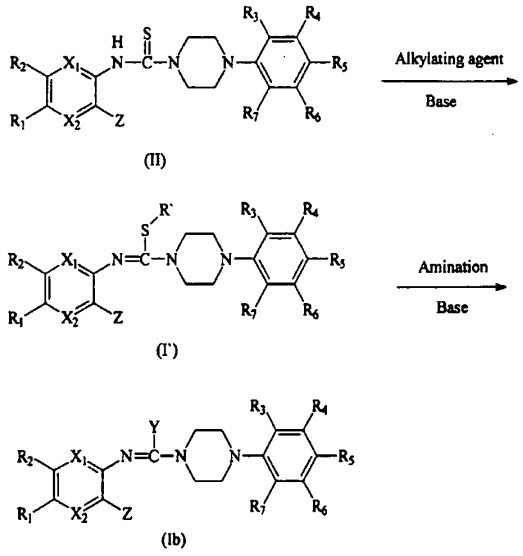
The conventional inorganic or organic base used in above step may include sodium hydride, potassium hydride, sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, cesium carbonate, sodium bicarbonate, potassium bicarbonate, triethylamine, pyridine and DBU.

In the above reaction process, if any acid material is formed, a basic material may be added as a scavenger in order to eliminate the acid material from the reaction phase. Such basic material may be alkali metal hydroxide, alkali earth metal hydroxide, alkali metal oxide, alkali earth metal oxide, alkali metal carbonate, alkali earth metal carbonate, alkali metal hydrogen carbonate, alkali earth metal hydrogen carbonate such as for example, sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, magnesium oxide, calcium oxide, potassium carbonate, sodium carbonate, calcium carbonate, magnesium carbonate, magnesium bicarbonate, sodium bicarbonate, calcium bicarbonate or the like, and organic amines.

The compounds of the general formula (2) and the formula (4) are known compounds, or may be prepared by a known method described in, for example, Farmaco(pavia) Ed, Sci., 18(8), 557-65(1963) or by a similar method thereto.

A compound of the general formula (I) wherein —C=Y— forms a single bond and —N=C— forms a double bond may be prepared by the following scheme II

Scheme II.



wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, X_1, X_2, Y and Z are as defined above, and R' is lower alkyl such as methyl and ethyl.

A compound of the general formula (II), which may be prepared by a known method, is reacted with an alkylating agent in the presence of a base to give a compound of the general formula (I'). Then, the compound of the formula (I') is reacted with a substituted or unsubstitued amine in the presence of a base to give a compound of the general formula (Ib).

The reaction may be carried out at a temperature between 3℃ and

boiling point of the solvent used, preferably at 50℃-100℃ for 5 - 48 hours, preferably for 10 - 24 hours.

The alkylating agent may be used in an amount of 1 - 1.5 equivalent to the compound (II). The alkylating agent may include C_1-C_8 alkyl halide, C_1-C_8 alkylsulfonate, substituted or unsubstituted C_3-C_8 cycloalkyl halide, aryl halide and substituted or unsubstituted C_3-C_8 cycloalkyl sulfonate.

The reaction may be carried out in a conventional organic solvent as described above.

The conventional inorganic or organic base as described above may be used in the above process.

The compound of the formula (I') is reacted with a substituted or unsubstitued amine in the presence of a conventional base to give a compound of the general formula (Ib).

The reaction also may be preferably carried out in a conventional organic solvent as decribed above.

The conventional inorganic or organic base described above may be used in the above reaction step.

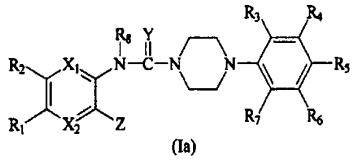
In the above reactions, if any acid material is formed, any basic material may be preferably added as a scavenger in order to eliminate the acid material from the reaction phase. Such basic material may be the organic or inorganic bases as described in the scheme I above.

The compound of the general formula (II) is a known compound, or may be prepared by a known method described in, for example, USP 5,780,472, PCT/KR97/00128 or by a similar method thereto.

Hereinafter the present invention will be described in more details with reference to following examples but it is not intended to limit the scope of the invention thereinto.

Compounds of the general formula (Ia) were prepared in following

examples according to the above-mentioned process.



(Ia)

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, X_1, X_2, Y and Z are as defined above.

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	X_1	X_2	Y	Z
1	CH_3	CH_3	H	H	H	H	H	H	N	N	O	OCH_3
2	CH_3	CH_3	OCH_3	H	H	H	H	H	N	N	O	OCH_3
3	CH_3	CH_3	H	OCH_3	H	OCH_3	H	H	N	N	O	OCH_3
4	CH_3	CH_3	Et	H	H	H	H	H	N	N	O	OCH_3
5	CH_3	CH_3	H	H	n-Bu	H	H	H	N	N	O	OCH_3
6	CH_3	CH_3	iPr	H	H	H	H	H	N	N	O	OCH_3
7	CH_3	CH_3	H	CH_3	H	CH_3	H	H	N	N	O	OCH_3
8	CH_3	CH_3	CH_3	CH_3	H	CH_3	CH_3	H	N	N	O	OCH_3
9	CH_3	CH_3	F	H	H	H	H	H	N	N	O	OCH_3
10	CH_3	CH_3	H	Br	H	H	H	H	N	N	O	OCH_3
11	CH_3	CH_3	H	Cl	H	Cl	H	H	N	N	O	OCH_3
12	CH_3	CH_3	H	F	H	F	H	H	N	N	O	OCH_3
13	CH_3	CH_3	H	CF_3	H	H	H	H	N	N	O	OCH_3
14	CH_3	CH_3	SCH_3	H	H	H	H	H	N	N	O	OCH_3
15	CH_3	CH_3	H	NO_2	H	NO_2	H	H	N	N	O	OCH_3

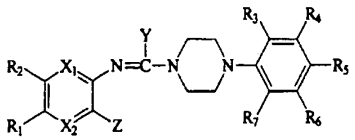
Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	X_1	X_2	Y	Z
16	CH_3	CH_3	H	NH_2	H	NH_2	H	H	N	N	O	OCH_3
17	CH_3	CH_3	H	H	Ac	H	H	H	N	N	O	OCH_3
18	CH_3	CH_3	OCH_3	H	H	H	H	CH_3	N	N	O	OCH_3
19	CH_3	CH_3	H	OCH_3	H	OCH_3	H	CH_3	N	N	O	OCH_3
20	CH_3	CH_3	H	CH_3	H	CH_3	H	CH_3	N	N	O	OCH_3
21	CH_3	CH_3	H	Cl	H	Cl	H	CH_3	N	N	O	OCH_3
22	CH_3	CH_3	H	F	H	F	H	CH_3	N	N	O	OCH_3
23	CH_3	CH_3	SCH_3	H	H	H	H	CH_3	N	N	O	OCH_3
24	CH_3	CH_3	H	NO_2	H	NO_2	H	CH_3	N	N	O	OCH_3
25	CH_3	CH_3	H	NH_2	H	NH_2	H	CH_3	N	N	O	OCH_3
26	CH_3	CH_3	H	OCH_3	H	OCH_3	H	Et	N	N	O	OCH_3
27	CH_3	CH_3	H	CH_3	H	CH_3	H	Et	N	N	O	OCH_3
28	CH_3	CH_3	H	OCH_3	H	OCH_3	H	H	N	N	S	OCH_3
29	CH_3	CH_3	Et	H	H	H	H	H	N	N	S	OCH_3
30	CH_3	CH_3	H	CH_3	H	CH_3	H	H	N	N	S	OCH_3
31	CH_3	CH_3	H	Br	H	H	H	H	N	N	S	OCH_3
32	CH_3	CH_3	H	Cl	H	Cl	H	H	N	N	S	OCH_3
33	CH_3	CH_3	SCH_3	H	H	H	H	H	N	N	S	OCH_3
34	Et	Et	H	CH_3	H	CH_3	H	H	N	N	O	OCH_3
35	Et	Et	H	OCH_3	H	OCH_3	H	H	N	N	O	OCH_3

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	X_1	X_2	Y	Z
36	CH=CH-CH=CH		H	H	H	H	H	H	N	N	O	OCH_3
37	CH=CH-CH=CH		OCH_3	H	H	H	H	H	N	N	O	OCH_3
38	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	H	N	N	O	OCH_3
39	CH=CH-CH=CH		Et	H	H	H	H	H	N	N	O	OCH_3
40	CH=CH-CH=CH		iPr	H	H	H	H	H	N	N	O	OCH_3
41	CH=CH-CH=CH		H	H	nBu	H	H	H	N	N	O	OCH_3
42	CH=CH-CH=CH		H	CH_3	H	CH_3	H	H	N	N	O	OCH_3
43	CH=CH-CH=CH		CH_3	CH_3	H	CH_3	CH_3	H	N	N	O	OCH_3
44	CH=CH-CH=CH		F	H	H	H	H	H	N	N	O	OCH_3
45	CH=CH-CH=CH		H	Br	H	H	H	H	N	N	O	OCH_3
46	CH=CH-CH=CH		H	F	H	F	H	H	N	N	O	OCH_3
47	CH=CH-CH=CH		H	CF_3	H	H	H	H	N	N	O	OCH_3
48	CH=CH-CH=CH		H	NO_2	H	NO_2	H	H	N	N	O	OCH_3
49	CH=CH-CH=CH		H	NH_2	H	NH_2	H	H	N	N	O	OCH_3
50	CH=CH-CH=CH		H	H	Ac	H	H	H	N	N	O	OCH_3
51	CH=CH-CH=CH		SCH_3	H	H	H	H	H	N	N	O	OCH_3
52	CH=CH-CH=CH		Ph	H	H	H	H	H	N	N	O	OCH_3
53	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	CH_3	N	N	O	OCH_3
54	CH=CH-CH=CH		OCH_3	H	H	H	H	CH_3	N	N	O	OCH_3
55	CH=CH-CH=CH		H	CH_3	H	CH_3	H	CH_3	N	N	O	OCH_3

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	X_1	X_2	Y	Z
56	CH=CH-CH=CH		H	F	H	F	H	CH_3	N	N	O	OCH_3
57	CH=CH-CH=CH		H	NO_2	H	NO_2	H	CH_3	N	N	O	OCH_3
58	CH=CH-CH=CH		H	NH_2	H	NH_2	H	CH_3	N	N	O	OCH_3
59	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	Et	N	N	O	OCH_3
60	CH=CH-CH=CH		H	CH_3	H	CH_3	H	Et	N	N	O	OCH_3
61	CH=CH-CH=CH		H	Cl	H	Cl	H	Et	N	N	O	OCH_3
62	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	iPr	N	N	O	OCH_3
63	CH=CH-CH=CH		OCH_3	H	H	H	H	H	N	N	S	OCH_3
64	CH=CH-CH=CH		F	OCH_3	H	OCH_3	H	H	N	N	S	OCH_3
65	CH=CH-CH=CH		Et	H	H	H	H	H	N	N	S	OCH_3
66	CH=CH-CH=CH		H	CH_3	H	CH_3	H	H	N	N	S	OCH_3
67	CH=CH-CH=CH		H	Br	H	H	H	H	N	N	S	OCH_3
68	CH=CH-CH=CH		H	F	H	F	H	H	N	N	S	OCH_3
69	CH=CH-CH=CH		SCH_3	H	H	H	H	H	N	N	S	OCH_3
70	CH=CH-CH=CH		H	H	Ac	H	H	H	N	N	S	OCH_3
71	CH=CH-CH=CH		H	H	nBu	H	H	H	N	N	S	OCH_3
72	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	H	N	N	O	OEt
73	CH=CH-CH=CH		OEt	H	H	H	H	H	N	N	O	OEt
74	CH=CH-CH=CH		H	CH_3	H	CH_3	H	H	N	N	O	OEt
75	CH=CH-CH=CH		CH_3	CH_3	H	H	H	H	N	N	O	OEt

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	X_1	X_2	Y	Z
76	CH=CH-CH=CH		Et	H	H	H	H	H	N	N	O	OEt
77	CH=CH-CH=CH		H	Cl	H	Cl	H	H	N	N	O	OEt
78	CH=CH-CH=CH		H	Br	H	H	H	H	N	N	O	OEt
79	CH=CH-CH=CH		H	F	H	F	H	H	N	N	O	OEt
80	CH=CH-CH=CH		SCH_3	H	H	H	H	H	N	N	O	OEt
81	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	CH_3	N	N	O	OEt
82	CH=CH-CH=CH		H	Cl	H	Cl	H	CH_3	N	N	O	OEt
83	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	Et	N	N	O	OEt
84	CH=CH-CH=CH		H	Cl	H	Cl	H	Et	N	N	O	OEt
85	CH=CH-CH=CH		H	CH_3	H	CH_3	H	Et	N	N	O	OEt
86	CH=CH-CH=CH		H	CH_3	H	CH_3	H	H	C	C	O	OCH_3
87	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	H	C	C	O	OCH_3
88	CH=CH-CH=CH		H	F	H	F	H	H	C	C	O	OCH_3
89	CH=CH-CH=CH		H	Cl	H	Cl	H	H	C	C	O	OCH_3
90	CH=CH-CH=CH		H	CH_3	H	CH_3	H	CH_3	C	C	O	OCH_3
91	CH=CH-CH=CH		H	F	H	F	H	CH_3	C	C	O	OCH_3
92	CH=CH-CH=CH		H	Cl	H	Cl	H	CH_3	C	C	O	OCH_3
93	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	CH_3	C	C	O	OCH_3
94	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	Et	C	C	O	OCH_3
95	CH=CH-CH=CH		H	CH_3	H	CH_3	H	Et	C	C	O	OCH_3

The compounds of the general formula (Ib) were prepared in the following examples according to the above-described process.



(Ib)

wherein, R_1, R_2, R_3, R_4, R_5, R_6, R_7, X, Y and Z are as defined above.

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	X_1	X_2	Y	Z
96	CH_3	CH_3	H	H	H	H	H	C	N	NHOH	OCH_3
97	CH_3	CH_3	H	H	CH_3	H	H	C	N	NHOH	OCH_3
98	CH_3	CH_3	H	H	nBu	H	H	C	N	NHOH	OCH_3
99	CH_3	CH_3	H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3
100	CH_3	CH_3	OCH_3	H	H	H	H	C	N	NHOH	OCH_3
104	CH_3	CH_3	H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
102	CH_3	CH_3	H	F	H	F	H	C	N	NHOH	OCH_3
103	CH_3	CH_3	H	Cl	H	Cl	H	C	N	NHOH	OCH_3
104	CH_3	CH_3	H	Br	H	H	H	C	N	NHOH	OCH_3
105	CH_3	CH_3	H	NO_2	H	NO_2	H	C	N	NHOH	OCH_3
106	CH_3	CH_3	H		H		H	C	N	NHOH	OCH_3
107	CH_3	CH_3	H		H		H	C	N	NHOH	OCH_3
108	CH_3	Et	OCH_3	H	H	H	H	C	N	NHOH	OCH_3
109	CH_3	Et	H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
110	CH_3	Et	Et	H	H	H	H	C	N	NHOH	OCH_3

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	X_1	X_2	Y	Z
111	CH_3	Et	H	H	H	H	H	C	N	NHOH	OCH_3
112	CH_3	Et	SCH_3	H	H	H	H	C	N	NHOH	OCH_3
113	CH_3	Et	H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3
114	CH_3	Et	H	F	H	F	H	C	N	NHOH	OCH_3
115	CH_3	Et	H	Cl	H	Cl	H	C	N	NHOH	OCH_3
116	CH_3	Et	Ph	H	H	H	H	C	N	NHOH	OCH_3
117	CH_3	Et	H	NO_2	H	NO_2	H	C	N	NHOH	OCH_3
118	CH_3		H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
119	CH_3		H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3
120	CH_3		H	F	H	F	H	C	N	NHOH	OCH_3
121	CH_3		OCH_3	H	H	H	H	C	N	NHOH	OCH_3
122	CH_3		H	H	H	H	H	C	N	NHOH	OCH_3
123	CH_3		H	H	CH_3	H	H	C	N	NHOH	OCH_3
124	CH_3		H	Cl	H	H	H	C	N	NHOH	OCH_3
125	CH_3		H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
126	CH_3		H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3
127	CH_3		H	F	H	F	H	C	N	NHOH	OCH_3
128	CH_3		OCH_3	H	H	H	H	C	N	NHOH	OCH_3
129	CH_3		H	H	H	H	H	C	N	NHOH	OCH_3
130	CH_3		H	H	CH_3	H	H	C	N	NHOH	OCH_3

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	X_1	X_2	Y	Z
131	CH_3		H	Cl	H	H	H	C	N	NHOH	OCH_3
132	CH_3		H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3
133	CH_3		H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
134	CH_3		H	H	H	H	H	C	N	NHOH	OCH_3
135	CH_3		H	H	CH_3	H	H	C	N	NHOH	OCH_3
136	CH_3		H	F	H	F	H	C	N	NHOH	OCH_3
137	CH_3		SCH_3	H	H	H	H	C	N	NHOH	OCH_3
138	CH_3		H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3
139	CH_3		H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
140	CH_3		H	H	H	H	H	C	N	NHOH	OCH_3
141	CH_3		H	H	CH_3	H	H	C	N	NHOH	OCH_3
142	CH_3		H	F	H	F	H	C	N	NHOH	OCH_3
143	CH_3		SCH_3	H	H	H	H	C	N	NHOH	OCH_3
144	CH_3		H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3
145	CH_3		H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
146	CH_3		H	F	H	F	H	C	N	NHOH	OCH_3
147	CH_3		SCH_3	H	H	H	H	C	N	NHOH	OCH_3
148	CH_3		H	NO_2	H	NO_2	H	C	N	NHOH	OCH_3
149	CH_3		H	H	CH_3	H	H	C	N	NHOH	OCH_3
150	CH_3		H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	X_1	X_2	Y	Z
151	CH_3		H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
152	CH_3		H	F	H	F	H	C	N	NHOH	OCH_3
153	CH_3		SCH_3	H	H	H	H	C	N	NHOH	OCH_3
154	CH_3		H	NO_2	H	NO_2	H	C	N	NHOH	OCH_3
155	CH_3		H	Cl	H	Cl	H	C	N	NHOH	OCH_3
156	Et		H	H	CH_3	H	H	C	N	NHOH	OCH_3
157	Et		Et	H	H	H	H	C	N	NHOH	OCH_3
158	Et		H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3
159	Et		H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
160	Et		H	Cl	H	Cl	H	C	N	NHOH	OCH_3
161	Et		SCH_3	H	H	H	H	C	N	NHOH	OCH_3
162	Et		H		H		H	C	N	NHOH	OCH_3
163	Et		H	F	H	F	H	C	N	NHOH	OCH_3
164	Et		H	H	CH_3	H	H	C	N	NHOH	OCH_3
165	Et		Et	H	H	H	H	C	N	NHOH	OCH_3
166	Et		H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3
167	Et		H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
168	Et		H	Cl	H	Cl	H	C	N	NHOH	OCH_3
169	Et		SCH_3	H	H	H	H	C	N	NHOH	OCH_3
170	Et		H		H		H	C	N	NHOH	OCH_3

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	X_1	X_2	Y	Z
171	Et		H	F	H	F	H	C	N	NHOH	OCH_3
172	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	C	N	NHOH	OCH_3
173	CH=CH-CH=CH		H	CH_3	H	CH_3	H	C	N	NHOH	OCH_3
174	CH=CH-CH=CH		H	F	H	F	H	C	N	NHOH	OCH_3
175	CH=CH-CH=CH		OCH_3	H	H	H	H	C	N	NHOH	OCH_3
176	CH=CH-CH=CH		H	Cl	H	H	H	C	N	NHOH	OCH_3
177	CH_3	CH_3	H	H	H	H	H	C	C	NHOH	OCH_3
178	CH_3	CH_3	H	H	CH_3	H	H	C	C	NHOH	OCH_3
179	CH_3	CH_3	Et	H	H	H	H	C	C	NHOH	OCH_3
180	CH_3	CH_3	H	CH_3	H	CH_3	H	C	C	NHOH	OCH_3
181	CH_3	CH_3	H	OCH_3	H	OCH_3	H	C	C	NHOH	OCH_3
182	CH_3	CH_3	H	F	H	F	H	C	C	NHOH	OCH_3
183	CH_3	CH_3	H	Cl	H	H	H	C	C	NHOH	OCH_3
184	CH_3	CH_3	H	Br	H	H	H	C	C	NHOH	OCH_3
185	CH_3	CH_3	SCH_3	H	H	H	H	C	C	NHOH	OCH_3
186	CH_3	CH_3	H	H	H	H	H	C	N	$NHOCH_3$	OCH_3
187	CH_3	CH_3	H	H	CH_3	H	H	C	N	$NHOCH_3$	OCH_3
188	CH_3	CH_3	H	CH_3	H	CH_3	H	C	N	$NHOCH_3$	OCH_3
189	CH_3	CH_3	H	OCH_3	H	OCH_3	H	C	N	$NHOCH_3$	OCH_3
190	CH_3	CH_3	H	F	H	F	H	C	N	$NHOCH_3$	OCH_3

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	X_1	X_2	Y	Z
191	CH_3	CH_3	SCH_3	H	H	H	H	C	N	$NHOCH_3$	OCH_3
192	CH_3	CH_3	H	NO_2	H	NO_2	H	C	N	$NHOCH_3$	OCH_3
193	CH_3	Et	H	Cl	H	Cl	H	C	N	$NHOCH_3$	OCH_3
194	Et		H	F	H	F	H	C	N	$NHOCH_3$	OCH_3
195	Et		H		H		H	C	N	$NHOCH_3$	OCH_3
196	Et		H		H		H	C	N	$NHOCH_3$	OCH_3
197	CH_3	CH_3	H	H	CH_3	H	H	C	C	$NHOCH_3$	OCH_3
198	CH_3	CH_3	H	CH_3	H	CH_3	H	C	C	$NHOCH_3$	OCH_3
199	CH_3	CH_3	H	H	H	H	H	C	N	SCH_3	OCH_3
200	CH_3	CH_3	H	H	CH_3	H	H	C	N	SCH_3	OCH_3
201	CH_3	CH_3	H	H	nBu	H	H	C	N	SCH_3	OCH_3
202	CH_3	CH_3	H	CH_3	H	CH_3	H	C	N	SCH_3	OCH_3
203	CH_3	CH_3	OCH_3	H	H	H	H	C	N	SCH_3	OCH_3
204	CH_3	CH_3	H	OCH_3	H	OCH_3	H	C	N	SCH_3	OCH_3
205	CH_3	CH_3	H	F	H	F	H	C	N	SCH_3	OCH_3
206	CH_3	CH_3	H	Cl	H	Cl	H	C	N	SCH_3	OCH_3
207	CH_3	CH_3	H	Br	H	H	H	C	N	SCH_3	OCH_3
208	CH_3	CH_3	H	NO_2	H	NO_2	H	C	N	SCH_3	OCH_3
209	CH_3	CH_3	H		H		H	C	N	SCH_3	OCH_3
210	CH_3	Et	H	H	H	H	H	C	N	SCH_3	OCH_3

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	X_1	X_2	Y	Z
211	CH_3	Et	OCH_3	H	H	H	H	C	N	SCH_3	OCH_3
212	CH_3	Et	H	OCH_3	H	OCH_3	H	C	N	SCH_3	OCH_3
213	CH_3	Et	Et	H	H	H	H	C	N	SCH_3	OCH_3
214	CH_3	Et	H	CH_3	H	CH_3	H	C	N	SCH_3	OCH_3
215	CH_3	Et	H	F	H	F	H	C	N	SCH_3	OCH_3
216	CH_3	Et	H	Cl	H	Cl	H	C	N	SCH_3	OCH_3
217	CH_3	Et	Ph	H	H	H	H	C	N	SCH_3	OCH_3
218	CH_3	Et	H	NO_2	H	NO_2	H	C	N	SCH_3	OCH_3
219	CH_3	Et	SCH_3	H	H	H	H	C	N	SCH_3	OCH_3
220	CH_3		H	OCH_3	H	OCH_3	H	C	N	SCH_3	OCH_3
221	CH_3		H	CH_3	H	CH_3	H	C	N	SCH_3	OCH_3
222	CH_3		H	F	H	F	H	C	N	SCH_3	OCH_3
223	CH_3		OCH_3	H	H	H	H	C	N	SCH_3	OCH_3
224	CH_3		H	H	H	H	H	C	N	SCH_3	OCH_3
225	CH_3		H	H	CH_3	H	H	C	N	SCH_3	OCH_3
226	CH_3		H	Cl	H	H	H	C	N	SCH_3	OCH_3
227	CH_3		H	CH_3	H	CH_3	H	C	N	SCH_3	OCH_3
228	CH_3		H	OCH_3	H	OCH_3	H	C	N	SCH_3	OCH_3
229	CH_3		H	H	H	H	H	C	N	SCH_3	OCH_3
230	CH_3		H	H	CH_3	H	H	C	N	SCH_3	OCH_3

Ex.	R_1	R_2	R_3	R_4	R_5	R_6	R_7	X_1	X_2	Y	Z
231	CH_3		H	F	H	F	H	C	N	SCH_3	OCH_3
232	CH_3		SCH_3	H	H	H	H	C	N	SCH_3	OCH_3
233	Et		H	H	CH_3	H	H	C	N	SCH_3	OCH_3
234	Et		Et	H	H	H	H	C	N	SCH_3	OCH_3
235	Et		H	CH_3	H	CH_3	H	C	N	SCH_3	OCH_3
236	Et		H	OCH_3	H	OCH_3	H	C	N	SCH_3	OCH_3
237	Et		H	Cl	H	Cl	H	C	N	SCH_3	OCH_3
238	Et		SCH_3	H	H	H	H	C	N	SCH_3	OCH_3
239	Et		H		H		H	C	N	SCH_3	OCH_3
240	Et		H	F	H	F	H	C	N	SCH_3	OCH_3
241	CH=CH-CH=CH		H	OCH_3	H	OCH_3	H	C	N	SCH_3	OCH_3
242	CH=CH-CH=CH		H	CH_3	H	CH_3	H	C	N	SCH_3	OCH_3
243	CH=CH-CH=CH		H	F	H	F	H	C	N	SCH_3	OCH_3
244	CH=CH-CH=CH		OCH_3	H	H	H	H	C	N	SCH_3	OCH_3
245	CH=CH-CH=CH		H	Cl	H	H	H	C	N	SCH_3	OCH_3
246	CH_3	CH_3	H	H	H	H	H	C	C	SCH_3	OCH_3
247	CH_3	CH_3	H	H	CH_3	H	H	C	C	SCH_3	OCH_3
248	CH_3	CH_3	Et	H	H	H	H	C	C	SCH_3	OCH_3
249	CH_3	CH_3	H	CH_3	H	CH_3	H	C	C	SCH_3	OCH_3
250	CH_3	CH_3	H	OCH_3	H	OCH_3	H	C	C	SCH_3	OCH_3

Ex	R_1	R_2	R_3	R_4	R_5	R_6	R_7	X_1	X_2	Y	Z
251	CH_3	CH_3	H	F	H	F	H	C	C	SCH_3	OCH_3
252	CH_3	CH_3	H	Cl	H	H	H	C	C	SCH_3	OCH_3
253	CH_3	CH_3	H	Br	H	H	H	C	C	SCH_3	OCH_3
254	CH_3	CH_3	SCH_3	H	H	H	H	C	C	SCH_3	OCH_3

Example 1)

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-phenylpiperazine

a) Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate:

3-Amino-5,6-dimethyl-2-methoxypyrazine(1.00g, 6.53mmol) and phenylchloroformate(1.02g, 6.53mmol) were dissolved in dichloromethane and stirred at room temperature for 2 hours. The resulting mixture was concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield: 98 %

m.p.: 101~103℃

b) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-phenyl piperazine:

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate (350mg, 1.28mmol) and 1-phenylpiperazine(208mg, 1.28mmol) were dissolved in anhydrous tetrahydrofuran and thereto DBU(195mg, 1.28mmol) was added. The resulting mixture was stirred at room temperature for 2 hours and concentrated under the reduced pressure to remove the solvent, and purified by column chromatography to obtain the titled compound.

yield : 78.5%

m.p. : 185~187℃

Example 2) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(2-methoxyphenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(2-methoxyphenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 82.0%

m.p.: 184~185℃

Example 3) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(3,5-dimethoxyphenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 85.0%

m.p.: 136~137℃

Example 4) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(2-ethylphenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(2-ethylphenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 70.4%

m.p.: 197~199℃

Example 5) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(4-butylphenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(4-butylphenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 68.5%

m.p.: 121~123℃

Example 6) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(2-isopropylphenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and

1-(2-isopropylphenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 73.0%

m.p.: 165~167℃

Example 7) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(3,5-dimethylphenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 84.0%

m.p.: 162~164℃

Example 8) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(2,3,5,6-tetramethylphenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(2,3,5,6,-tetramethylphenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 65.5%

m.p.: 202~204℃

Example 9) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(2-fluorophenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(2-fluorophenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 74.5%

m.p.: 170~172℃

Example 10) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3-bromophenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(3-bromophenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 70.0%

m.p.: 158~160℃

Example 11) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dichlorophenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(3,5-dichlorophenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 80.5%

m.p.: 180~181℃

Example 12) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-difluorophenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(3,5-difluorophenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 78.0%

m.p.: 153~154℃

Example 13) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3-trifluorotolyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(3-trifluorotolyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 69.5%

m.p.: 168~170℃

Example 14) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(2-methylthiophenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(2-methylthiophenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 71.0%

m.p.: 202~204℃

Example 15) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dinitrophenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(3,5-dinitrophenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 64.5%

m.p.: 192~194℃

Example 16) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-diaminophenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dinitrophenyl)piperazine was dissolved in ethanol(30ml) and thereto 10% palladium/carbon(10mg) was added. The resulting mixture was hydrogenated for 4 hours, and then filtered to remove the 10% palladium/carbon. The filtrate was concentrated and purified by column chromatography to obtain the titled compound.

yield : 45.0%

m.p.: >100℃(decomposed)

Example 17) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(4-acetylphenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)carbamate and 1-(4-acetylphenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

Yield : 71.5%

m.p.: 166~168℃

Example 18) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl) N-methylamino-carbonyl]-4-(2-methoxyphenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(2-methoxyphenyl)piperazine(200mg, 0.54mmol) was dissolved in dimethylformamide (15ml) and thereto 60% sodium hydride (21.5mg, 0.54mmol) was added. The resulting mixture was stirred at room temperature for 15 minutes, and thereto methyl iodide(76.6mg, 0.54mmol) was added. The resulting mixture was stirred at room temperature for 6 hours, concentrated under the reduced pressure to remove the solvent,

and purified by column chromatography to obtain the titled compound.
yield: 92.5%
m.p.: 140~142℃

Example 19) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl) N-methylamino-carbonyl]-4-(3,5-dimethoxyphenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine was reacted by the same way with the example 18 to obtain the titled compound.
yield: 90.5%
m.p.: 80~82℃

Example 20) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl) N-methylamino-carbonyl]-4-(3,5-dimethylphenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl)piperazine was reacted by the same way with the example 18 to obtain the titled compound.
yield: 88.4%
m.p.: 94~96℃

Example 21) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl) N-methylamino-carbonyl]-4-(3,5-dichlorophenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dichlorophenyl)piperazine was reacted by the same way with the example 18 to obtain the titled compound.
yield: 95.2%
m.p.: 97~99℃

Example 22) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl) N-methylamino-carbonyl]-4-(3,5-difluorophenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-difluorophenyl)piperazine was reacted by the same way with the example 18 to obtain the titled compound.
yield: 94.0%
m.p.: 104~106℃

Example 23) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl) N-methylamino-carbonyl]-4-(2-methylthiophenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(2-methylthiophenyl)piperazine was reacted by the same way with the example 18 to obtain the titled compound.

yield: 89.5%

m.p.: 133~134℃

Example 24) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl) N-methylamino-carbonyl]-4-(3,5-dinitrophenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dinitrophenyl)piperazine was reacted by the same way with the example 18 to obtain the titled compound.

yield: 80.0%

m.p.: 133~135℃

Example 25) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl) N-methylamino-carbonyl]-4-(3,5-diaminophenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)N-methylaminocarbonyl]-4-(3,5-dinitrophenyl)piperazine was reacted by the same way with the example 18 to obtain the titled compound.

yield: 58.5%

m.p.: >100℃(decomposed)

Example 26) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl) N-ethylamino-carbonyl]-4-(3,5-dimethoxyphenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine(250mg, 0.62mmol) was dissolved in dimethylformamide(20ml) and thereto 60% sodium hydride(24.9mg, 0.62mmol) was added. The mixture was stirred at room temperature for 15 minutes, and thereto methyl iodide(96.7mg, 0.62mmol) was added. The resulting mixture was stirred at room temperature for 6 hours, concentrated under the reduced pressure to remove the solvent used, and purified by column chromatography to obtain the titled compound.

yield: 89.5%

m.p.: 78~80℃

Example 27) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl) N-ethylamino-carbonyl]-4-(3,5-dimethylphenyl)piperazine

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl)piperazine was reacted by the same way with the example 26 to obtain the titled compound.

yield: 92.0%

m.p.: 68~70℃

Example 28)

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminothiocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine

a) Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)thiocarbamate:

3-Amino-5,6-dimethyl-2-methoxypyrazine(500mg, 3.26mmol) was dissolved in dichloromethane and thereto phenyl thiochloroformate (564mg, 3.26mmol) was slowly added. The mixture was stirred at room temperature for 24 hours, concentrated under the reduced pressure to remove the solvent, and purified by column chromatography to obtain the titled compound.

yield: 78.5%

m.p.: 71~73℃

b) 1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminothiocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine:

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)thiocarbamate (200mg, 0.69mmol) and 1-(3,5-dimethoxyphenyl)piperazine(154mg, 0.69mmol) were dissolved in anhydrous tetrahydrofuran(25ml) and thereto DBU(105mg, 0.69mmol) was added. The mixture was stirred at room temperature for 2 hours, concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield : 71.5%

m.p. : 183~184℃

Example 29)

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminothiocarbonyl]-4-(2-ethylphenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)thiocarbamate and 1-(2-ethylphenyl)piperazine were reacted by the same way with the example 28 to obtain the titled compound.

yield: 64.0%

m.p.: 197~199℃

Example 30)

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminothiocarbonyl]-4-(3,5-dimethylphenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)thiocarbamate and 1-(3,5-dimethylphenyl)piperazine were reacted by the same way with the example 28 to obtain the titled compound.

yield: 68.4%

m.p.: 160~162℃

Example 31)

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminothiocarbonyl]-4-(3-bromophenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)thiocarbamate and 1-(3-bromophenyl)piperazine were reacted by the same way with the example 28 to obtain the titled compound.

yield: 62.5%

m.p.: 136~138℃

Example 32)

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminothiocarbonyl]-4-(3,5-dichlorophenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)thiocarbamate and 1-(3,5-dichlorophenyl)piperazine were reacted by the same way with the example 28 to obtain the titled compound.

yield: 70.8%

m.p.: 182~184℃

Example 33)

1-[(5,6-Dimethyl-2-methoxypyrazin-3-yl)aminothiocarbonyl]-4-(2-methylthiophenyl)piperazine

Phenyl N-(5,6-dimethyl-2-methoxypyrazin-3-yl)thiocarbamate and 1-(2-methylthiophenyl)piperazine were reacted by the same way with the example 28 to obtain the titled compound.

yield: 61.4%

m.p.: 181~183℃

Example 34)

1-[(5,6-Dichloroethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl)piperazine

Phenyl N-(5,6-diethyl-2-methoxypyrazin-3-yl)carbamate and 1-(3,5-dimethylphenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 77.5%

m.p.: 118~120℃

Example 35)

1-[(5,6-Dichloroethyl-2-methoxypyrazin-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine

Phenyl N-(5,6-diethyl-2-methoxypyrazin-3-yl)carbamate and 1-(3,5-dimethoxyphenyl)piperazine were reacted by the same way with the example 1 to obtain the titled compound.

yield: 78.9%

m.p.: 90~92℃

Example 36)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-phenylpiperazine

a) Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate:

3-Amino-2-methoxyquinoxaline(1.00g, 6.53mmol) and phenylchloroformate (1.02g, 6.53mmol) were dissolved in dichloromethane and stirred at room temperature for 2 hours. The resulting mixture was

concentrated under the reduced pressure to remove the solvent, and purified by column chromatography to obtain the titled compound.

yield: 75.5%

m.p.: 147~149℃

b) 1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-phenylpiperazine:

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate(378mg, 1.28mmol) and 1-phenylpiperazine(208mg, 1.28mmol) were dissolved in anhydrous tetrahydrofuran and thereto DBU(195mg, 1.28mmol) was added. The mixture was stirred at room temperature for 2 hours, concentrated under the reduced pressure to remove the solvent, and purified by column chromatography to obtain the titled compound.

yield : 76.5%

m.p. : 156~158℃

Example 37)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-methoxyphenyl)-piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(2-methoxyphenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 72.4%

m.p. : 177~178℃

Example 38)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(3,5-dimethoxy-phenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 81.2%

m.p. : 140~141℃

Example 39)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-ethylphenyl)piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(2-ethylphenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 75.0%

m.p. : 191~193℃

Example 40)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-isoprop-ylphenyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(2-isopropylphenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 77.5%

m.p. : 147~149℃

Example 41)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(4-butylph-enyl)-piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(4-butylphenyl)-piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 65.4%

m.p. : 124~126℃

Example 42)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(3,5-dimethylphenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 79.3%

m.p. : 155~157℃

Example 43)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(2,3,5,6-tetramethyl-

phenyl)piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(2,3,5,6-tetramethylphenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 64.0%

m.p. : 237~239℃

Example 44)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-fluorop-henyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(2-fluorophenyl)-piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 67.5%

m.p. : 142~144℃

Example 45)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3-bromop-henyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(3-bromophenyl)-piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 69.5%

m.p. : 148~150℃

Example 46)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-difluo-rophenyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(3,5-difluorophenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 74.5%

m.p. : 172~173℃

Example 47)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-trifluorotolyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(2-trifluorotolyl)-piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 70.7%

m.p. : 132~134℃

Example 48)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dinitrophenyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(3,5-dinitrophenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 54.5%

m.p. : 216~218℃

Example 49)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-diami-nophenyl) piperazine

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dinitrophenyl) piperazine(200mg, 0.44mmol) was dissolved in ethanol(30ml) and thereto 10% palladium/carbon(10mg) was added. The mixture was hydrogenated for 4 hours, and then filtered to remove the 10% palladium/carbon. The filtrate was concentrated and purified by column chromatography to obtain the titled compound.

Yield : 42.5%

m.p.: >100℃(decomposed)

Example 50)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(4-acetylp-henyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(4-acetylphenyl)-piperazine were reacted by the same way with the

example 36 to obtain the titled compound.

yield : 71.0%

m.p. : 198~200℃

Example 51)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-methylt-hiophenyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(2-methylthiophenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 69.8%

m.p. : 180~182℃

Example 52)

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-biphen-yl)piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)carbamate and 1-(2-biphenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 59.0%

m.p. : 162~165℃

Example 53) 1-[(2-Methoxyquinoxalin-3-yl) N-methylaminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-methoxyphenyl) piperazine(229mg, 0.54mmol) was dissolved in dimethylformamide(15ml) and thereto 60% sodium hydride(21.5mg, 0.54mmol) was added. The mixture was stirred at room temperature for 15 minutes, and thereto ehtyl iodide (76.6mg, 0.54mmol) was added. The mixture was stirred at room temperature for 6 hours, concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield : 92.5%

m.p. : 143~144℃

Example 54) 1-[(2-Methoxyquinoxalin-3-yl) N-methylaminocarbonyl]-4-

(2-methoxyphenyl)piperazine

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-methoxyphenyl) piperazine was reacted by the same way with the example 53 to obtain the titled compound.

yield : 83.8%

m.p. : 128~130℃

Example 55) 1-[(2-Methoxyquinoxalin-3-yl) N-methylaminocarbonyl]-4-(3,5-dimethylphenyl)piperazine

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl) piperazine was reacted by the same way with the example 53 to obtain the titled compound.

yield : 86.5%

m.p. : 142~144℃

Example 56) 1-[(2-Methoxyquinoxalin-3-yl) N-methylaminocarbonyl]-4-(3,5-difluorophenyl)piperazine

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-difluorophenyl) piperazine was reacted by the same way with the example 53 to obtain the titled compound.

yield : 84.7%

m.p. : 197~199℃

Example 57) 1-[(2-Methoxyquinoxalin-3-yl) N-methylaminocarbonyl]-4-(3,5-dinitrophenyl)piperazine

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dinitrophenyl) piperazine was reacted by the same way with the example 53 to obtain the titled compound.

yield : 56.5%

m.p. : 197~199℃

Example 58) 1-[(2-Methoxyquinoxalin-3-yl) N-methylaminocarbonyl]-4-(3,5-diaminophenyl)piperazine

. To 1-[(2-methoxyquinoxalin-3-yl) N-methylaminocarbonyl]-4-(3,5-dinitrophenyl)piperazine dissolved in ethanol(30ml), 10%

palladium/carbon (10mg) was added. The mixture was hydrogenated for 4 hours, and then filtered to remove the 10% palladium/carbon. The filtrate was concentrated and purified by column chromatography to obtain the titled compound.

Yield : 44.5%

m.p.: >100℃(decomposed)

Example 59) 1-[(2-Methoxyquinoxalin-3-yl) N-ethylaminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine

To 1-[(2-methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine(263mg, 0.62mmol) dissolved in dimethylformamide (20ml), 60% sodium hydride(24.9mg, 0.62mmol) was added and stirred at room temperature for 15 minutes, and thereto methyl iodide (96.7mg, 0.62mmol) was added. The resulting mixture was stirred at room temperature for 6 hours, concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield : 85.4%

m.p. : 129~130℃

Example 60) 1-[(2-Methoxyquinoxalin-3-yl) N-ethylaminocarbonyl]-4-(3,5-dimethylphenyl)piperazine

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl) piperazine was reacted by the same way with the example 59 to obtain the titled compound.

yield : 87.6%

m.p. : 145~147℃

Example 61) 1-[(2-Methoxyquinoxalin-3-yl) N-ethylaminocarbonyl]-4-(3,5-dichlorophenyl)piperazine

1-[(2-Methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dichlorophenyl) piperazine were reacted by the same way with the example 59 to obtain the titled compound.

yield : 80.6%

m.p. : 146~148℃

Example 62) 1-[(2-Methoxyquinoxalin-3-yl) N-isopropylaminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine

To 1-[(2-methoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine(216mg, 0.51mmol) dissolved in dimethylformamide(20ml), 60% sodium hydride(20.4mg, 0.51mmol) was added and stirred at room temperature for 15 minutes, and thereto propyl iodide (86.7mg, 0.51mmol) was added. The resulting mixture was stirred at room temperature for 6 hours, concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield : 82.0%

m.p. : 110~112℃

Example 63)

1-[(2-Methoxyquinoxalin-3-yl)aminothiocarbonyl]-4-(2-met-hoxyphenyl) piperazine

a) Phenyl N-(2-Methoxyquinoxalin-3-yl)thiocarbamate:

To 3-Amino-2-Methoxyquinoxaline(571mg, 3.26mmol) dissolved in dichloromethane, phenylthiochloroformate(564mg, 3.26mmol) were added slowly and stirred at room temperature for 24 hours. The resulting mixture was concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield: 60.5%

m.p.: 160~162℃

b)

1-[(2-Methoxyquinoxalin-3-yl)aminothiocarbonyl]-4-(2-methoxyphenyl) piperazine:

Phenyl N-(2-methoxyquinoxalin-3-yl)thiocarbamate(215mg, 0.69mmol) and 1-(2-methoxyphenyl)piperazine(154mg, 0.69mmol) were dissolved in anhydrous tetrahydrofuran(25ml) and thereto DBU(105mg, 0.69mmol)

was added. The mixture was stirred at room temperature for 2 hours, concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield : 62.4%

m.p. : 177~179℃

Example 64)

1-[(2-Methoxyquinoxalin-3-yl)aminothiocarbonyl]-4-(3,5-dimethoxy-phenyl)piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)thiocarbamate and 1-(3,5-dimethoxyphenyl)piperazine were reacted by the same way with the example 63 to obtain the titled compound.

yield : 64.5%

m.p. : 141~143℃

Example 65)

1-[(2-Methoxyquinoxalin-3-yl)aminothiocarbonyl]-4-(2-ethylphenyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)thiocarbamate and 1-(2-ethylphenyl)piperazine were reacted by the same way with the example 63 to obtain the titled compound.

yield : 60.7%

m.p. : 141~143℃

Example 66)

1-[(2-Methoxyquinoxalin-3-yl)aminothiocarbonyl]-4-(3,5-di-methyl-phenyl)piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)thiocarbamate and 1-(3,5-dimethylphenyl)piperazine were reacted by the same way with the example 63 to obtain the titled compound.

yield : 65.0%

m.p. : 193~195℃

Example 67)

1-[(2-Methoxyquinoxalin-3-yl)aminothiocarbonyl]-4-(3-bro-mophenyl)

piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)thiocarbamate and 1-(3-bromophenyl)piperazine were reacted by the same way with the example 63 to obtain the titled compound.

yield : 57.5%

m.p. : 195~197℃

Example 68)

1-[(2-Methoxyquinoxalin-3-yl)aminothiocarbonyl]-4-(3,5-difluorophenyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)thiocarbamate and 1-(3,5-difluorophenyl)piperazine were reacted by the same way with the example 63 to obtain the titled compound.

yield : 59.0%

m.p. : 280~281℃

Example 69)

1-[(2-Methoxyquinoxalin-3-yl)aminothiocarbonyl]-4-(2-methylthio-phenyl)piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)thiocarbamate and 1-(2-methylthiophenyl)piperazine were reacted by the same way with the example 63 to obtain the titled compound.

yield : 64.5%

m.p. : 148~150℃

Example 70)

1-[(2-Methoxyquinoxalin-3-yl)aminothiocarbonyl]-4-(4-acetylphenyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)thiocarbamate and 1-(4-acetylphenyl)piperazine were reacted by the same way with the example 63 to obtain the titled compound.

yield : 56.9%

m.p. : 235~237℃

Example 71)

1-[(2-Methoxyquinoxalin-3-yl)aminothiocarbonyl]-4-(4-but-ylphenyl) piperazine

Phenyl N-(2-methoxyquinoxalin-3-yl)thiocarbamate and 1-(4-butylphenyl)piperazine were reacted by the same way with the example 63 to obtain the titled compound.

yield : 62.5%

m.p. : 163~165℃

Example 72)

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl) piperazine

Phenyl N-(2-ethoxyquinoxalin-3-yl)carbamate and 1-(3,5-dimethoxyphenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 74.7%

m.p. : 149~150℃

Example 73)

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-ethoxyphenyl) piperazine

Phenyl N-(2-ethoxyquinoxalin-3-yl)carbamate and 1-(2-ethoxyphenyl)-piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 76.5%

m.p. : 120~122℃

Example 74)

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl) piperazine

Phenyl N-(2-ethoxyquinoxalin-3-yl)carbamate and 1-(3,5-dimethylphenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 82.0%

m.p. : 152~154℃

Example 75)

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(2,3-dimethylphenyl) piperazine

Phenyl N-(2-ethoxyquinoxalin-3-yl)carbamate and 1-(2,3-dimethylphenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 78.7%

m.p. : 108~110℃

Example 76)

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-ethylphenyl)piperazine

Phenyl N-(2-ethoxyquinoxalin-3-yl)carbamate and 1-(2-ethylphenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 77.5%

m.p. : 152~154℃

Example 77)

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dichlorophenyl) piperazine

Phenyl N-(2-ethoxyquinoxalin-3-yl)carbamate and 1-(3,5-dichlorophenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 81.3%

m.p. : 157~159℃

Example 78)

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(3-bromophenyl)piperazine

Phenyl N-(2-ethoxyquinoxalin-3-yl)carbamate and 1-(3-bromophenyl)-piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 80.6%

m.p. : 164~166℃

Example 79)

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-difluorophenyl) piperazine

Phenyl N-(2-ethoxyquinoxalin-3-yl)carbamate and 1-(3,5-difluorophenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 78.6%

m.p. : 146~148℃

Example 80)

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(2-methylthiophenyl) piperazine

Phenyl N-(2-ethoxyquinoxalin-3-yl)carbamate and 1-(2-methylthiophenyl)piperazine were reacted by the same way with the example 36 to obtain the titled compound.

yield : 71.4%

m.p. : 139~141℃

Example 81) 1-[(2-Ethoxyquinoxalin-3-yl) N-methylaminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl)-piperazine was reacted by the same way with the example 53 to obtain the titled compound.

yield : 92.8%

m.p. : 159~161℃

Example 82) 1-[(2-Ethoxyquinoxalin-3-yl) N-methylaminocarbonyl]-4-(3,5-dichlorophenyl)piperazine

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dichlorophenyl) piperazine was reacted by the same way with the example 53 to obtain the titled compound.

yield : 94.5%

m.p. : 129~131℃

Example 83) 1-[(2-Ethoxyquinoxalin-3-yl) N-ethylaminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl)-piperazine was reacted by the same way with the example 61 to obtain the titled compound.

yield : 82.8%

m.p. : 144~146℃

Example 84) 1-[(2-Ethoxyquinoxalin-3-yl) N-ethylaminocarbonyl]-4-(3,5-dichlorophenyl)piperazine

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dichlorophenyl) piperazine was reacted by the same way with the example 61 to obtain the titled compound.

yield : 80.7%

m.p. : 115~117℃

Example 85) 1-[(2-Ethoxyquinoxalin-3-yl) N-ethylaminocarbonyl]-4-(3,5-dimethylphenyl)piperazine

1-[(2-Ethoxyquinoxalin-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl)-piperazine was reacted by the same way with the example 61 to obtain the titled compound.

yield : 78.8%

m.p. : 142~144℃

Example 86)

1-[(2-Methoxynaphth-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl)-piperazine

a) Phenyl N-(2-methoxynaphth-3-yl)carbamate:

3-Amino-2-methoxynaphthalene(1.13g, 6.53mmol) and phenylchloroformate(1.02g, 6.53mmol) were dissolved in dichloromethane. The mixture was stirred at room temperature for 2 hours, concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield: 75.0%

m.p.: 105~107℃

b) 1-[(2-Methoxynaphth-3-yl)aminothiocarbonyl]-4-(3,5-dimethylphenyl-

piperazine:

Phenyl N-(2-methoxynaphth-3-yl)carbamate(375mg, 1.28mmol) and 1-(3,5-dimethylphenyl)piperazine(208mg, 1.28mmol) were dissolved in anhydrous tetrahydrofuran(25ml) and thereto DBU(195mg, 1.28mmol) was added, and then stirred at room temperature for 2 hours, concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield : 72.0%

m.p. : 117~119℃

Example 87)

1-[(2-Methoxynaphth-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl) piperazine

Phenyl N-(2-methoxynaphth-3-yl)carbamate and 1-(3,5-dimethoxyphenyl)piperazine were reacted by the same way with the example 86 to obtain the titled compound.

yield : 74.5%

m.p. : 191~193℃

Example 88)

1-[(2-Methoxynaphth-3-yl)aminocarbonyl]-4-(3,5-difluorophenyl) piperazine

Phenyl N-(2-methoxynaphth-3-yl)carbamate and 1-(3,5-difluorophenyl)piperazine were reacted by the same way with the example 86 to obtain the titled compound.

yield : 78.5%

m.p. : 160~161℃

Example 89)

1-[(2-Methoxynaphth-3-yl)aminocarbonyl]-4-(3,5-dichlorophenyl) piperazine

Phenyl N-(2-methoxynaphth-3-yl)carbamate and 1-(3,5-dichlorophenyl)piperazine were reacted by the same way with the example 86 to obtain the titled compound.

yield : 76.7%

m.p. : 182~184℃

Example 90) 1-[(2-Methoxynaphth-3-yl)-N-methylaminocarbonyl]-4-(3,5-dimethylphenyl)piperazine

To 1-[(2-methoxynaphth-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl)-piperazine(210mg, 0.54mmol) dissolved in dimethylformamide(15ml), 60% sodium hydride(21.5mg, 0.54mmol) was added, stirred at room temperature for 15 minutes, and thereto methyl iodide (76.6mg, 0.54mmol) was added. The resulting mixture was stirred at room temperature for 6 hours, concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield : 86.4%

m.p. : 134~136℃

Example 91) 1-[(2-Methoxynaphth-3-yl)-N-methylaminocarbonyl]-4-(3,5-difluorophenyl)piperazine

1-[(2-Methoxynaphth-3-yl)aminocarbonyl]-4-(3,5-difluorophenyl)-piperazine was reacted by the same way with the example 90 to obtain the titled compound.

yield : 85.0%

m.p. : 115~117℃

Example 92) 1-[(2-Methoxynaphth-3-yl)-N-methylaminocarbonyl]-4-(3,5-dichlorophenyl)piperazine

1-[(2-Methoxynaphth-3-yl)aminocarbonyl]-4-(3,5-dichlorophenyl)-piperazine was reacted by the same way with the example 90 to obtain the titled compound.

yield : 89.8%

m.p. : 165~167℃

Example 93) 1-[(2-Methoxynaphth-3-yl)-N-methylaminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine

1-[(2-Methoxynaphth-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl)-

piperazine was reacted by the same way with the example 90 to obtain the titled compound.

yield : 92.5%

m.p. : 83~85℃

Example 94) 1-[(2-Methoxynaphth-3-yl)-N-ethylaminocarbonyl]-4-(3,5-dimethylphenyl)piperazine

To 1-[(2-methoxynaphth-3-yl)aminocarbonyl]-4-(3,5-dimethylphenyl) piperazine(210mg, 0.54mmol) dissolved in dimethylformamide(15ml), 60% sodium hydride(21.5mg, 0.54mmol) was added, stirred at room temperature for 15 minutes, and thereto methyl iodide (84.2mg, 0.54mmol) was added. The mixture was stirred at room temperature for 6 hours, concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield : 70.2%

Example 95) 1-[(2-Methoxynaphth-3-yl)-N-ethylaminocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine

1-[(2-Methoxynaphth-3-yl)aminocarbonyl]-4-(3,5-dimethoxyphenyl)-piperazine was reacted by the same way with the example 94 to obtain the titled compound.

yield : 85.0%

Example 96) N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-(4-phenylpiperazin-1-yl)carboxyimidamide

To methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-(4-phenyl-piperazin-1-yl)iminothiorate (0.50g, 1.35mmol) dissolved in chloroform (30ml), hydroxylamine hydrochlroride (0.25g, 3.60mmol) and triethylamine (0.41g, 4.05mmol) were added and stirred at room temperature for 15 hours, and then thereto water(30ml) was added to stop reaction. The resulting mixture was extracted with methylene chloride. The organic layer was concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield : 64.5%

m.p. : 173~175℃

Example 97) N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(4-methylphenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 55.2%

m.p. : 187~189℃

Example 98) N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(4-n-butylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(4-n-butylphenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 60.1%

m.p. : 153~155℃

Example 99) N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethylphenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 67.5%

m.p. : 125~128℃

Example 100)

N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(2-methoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(2-methoxyphenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 62.0%

m.p. : 134~136℃

Example 101) N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 57.2%

m.p. : 188~190℃

Example 102) N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 60.7%

m.p. : 177~178℃

Example 103) N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 65.4%

m.p. : 185~187℃

Example 104)

N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3-bromophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3-bromophenyl)-piperazine-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 68.1%

m.p. : 174~176℃

Example 105) N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dinitrophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dinitrophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 45.2%

m.p. : 193~195℃

Example 106) N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-diethylisophthal-1-yl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-diethylisophthal-1-yl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 64.1%

m.p. : 166~168℃

Example 107)

N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-{4-[3,5-bis-(hydroxymethyl)phenyl]piperazin-1-yl}carboxyimidamide

To N-hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[(4-(3,5-diethylisophthal-1-yl)piperazin-1-yl]carboxyimidamide (500mg, 1.0mmol) dissolved in tetrahydrofuran(20ml), lithium aluminium hydride (57mg, 1.5mmol) were added slowly, and stirred at 20℃ for 1 hours, and then thereto water(0.5ml) was added to stop reaction. The resulting mixture was concentrated under the reduced pressure to remove the solvent and extracted with methylene chloride with addition of water. The organic layer was dried with magnesium sulfate and purified by column chromatography to obtain the titled compound.

yield : 42.1%

m.p. : 184~186℃

Example 108)

N-Hydroxy-N'-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 69.4%

m.p. : 134~135℃

Example 109)

N-Hydroxy-N'-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 68.2%

m.p. : 140~142℃

Example 110)

N-Hydroxy-N'-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-ethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-ethylphen-yl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 70.2%

m.p. : 157~160℃

Example 111)

N-Hydroxy-N'-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-(4-phenylpiperazin-1-yl)carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-(4-phenylpiperazin-1-yl)iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 72.2%

m.p. : 178~180℃

Example 112)

N-Hydroxy-N'-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 69.3%

m.p. : 178~179℃

Example 113)

N-Hydroxy-N'-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 64.7%

m.p. : 155~157℃

Example 114)

N-Hydroxy-N'-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 51.8%

m.p. : 150~152℃

Example 115)

N-Hydroxy-N'-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 72.2%

m.p. : 172~174℃

Example 116)

N-Hydroxy-N'-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-biphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-biphenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 53.4%

m.p. : 195~197℃

Example 117)

N-Hydroxy-N'-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dinitrophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dinitro-phenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 44.3%

m.p. : 193~195℃

Example 118)

N-Hydroxy-N'-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 61.6%

m.p. : 192~194℃

Example 119)

N-Hydroxy-N'-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate was reacted by the

same way with the example 96 to obtain the titled compound.

yield : 63.0%

m.p. : 195~197℃

Example 120)

N-Hydroxy-N'-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 57.4%

m.p. : 170~172℃

Example 121)

N-Hydroxy-N'-(5-methoxycarbonyl-2-methoxy-6-methylpyridine-3-yl)-[4-(2-methoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 65.1%

m.p. : 176~178℃

Example 122)

N-Hydroxy-N'-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-(4-phenylpiperazin-1-yl)carboxyimidamide

Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-(4-phenylpiperazin-1-yl)iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 69.5%

m.p. : 194~196℃

Example 123)

N-Hydroxy-N'-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 73.2%

m.p. : 190~192℃

Example 124)

N-Hydroxy-N'-(5-methoxycarbonyl-2-methoxy-6-methylpyridine-3-yl)-[4-(3-chlorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3-chlorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 60.2%

m.p. : 91~93℃

Example 125)

N-Hydroxy-N'-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

To N-hydroxy-N'-(5-methoxycarbonyl-2-methoxy-6-methyl-pyridin-3-yl)-[(4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide (300mg, 0.65mmol) dissolved in tetrahydrofuran(20ml), lithium aluminium hydride(37mg, 0.98mmol) was added slowly and stirred at 20℃ for 1 hours. Then, water(0.5ml) was added thereto to stop reaction. The resulting mixture was concentrated under the reduced pressure to remove the solvent, and extracted with methylene chloride with addition of water. The organic layer was dried with magnesium sulfate, and purified by column chromatography to obtain the titled compound.

yield : 45.8%

m.p. : 185~187℃

Example 126)

N-Hydroxy-N'-(5-hydroxymethyl-2-methoxy-6-methylpyr-idine-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-

[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 47.3%

m.p. : 127~129℃

Example 127)

N-Hydroxy-N'-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 42.3%

m.p. : 179~181℃

Example 128)

N-Hydroxy-N'-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methoxyphenyl)piperazin-1-yl]carboxyimid-amide

Methyl N-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 57.5%

m.p. : 129~131℃

Example 129)

N-Hydroxy-N'-(5-hydroxymethyl-2-methoxy-6-methylpyr-idine-3-yl)-(4-phenylpiperazin-1-yl)carboxyimidamide

Methyl N-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-(4-phenylpiperazin-1-yl)iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 61.6%

m.p. : 167~169℃

Example 130)

N-Hydroxy-N'-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 66.7%

m.p. : 157~159℃

Example 131)

N-Hydroxy-N'-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3-chlorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-hydroxymethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3-chlorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 56.2%

m.p. : 171~173℃

Example 132)

N-Hydroxy-N'-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 35.1%

m.p. : 174~176℃

Example 133)

N-Hydroxy-N'-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 32.4%

m.p. : 143~145℃

Example 134)

N-Hydroxy-N'-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-(4-phenylpiperazin-1-yl)carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-(4-phenylpiperazin-1-yl)iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 40.5%

m.p. : 169~170℃

Example 135)

N-Hydroxy-N'-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 55.2%

m.p. : 164~166℃

Example 136)

N-Hydroxy-N'-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 33.2%

m.p. : 184~185℃

Example 137)

N-Hydroxy-N'-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 39.8%

m.p. : 178~179℃

Example 138)

N-Hydroxy-N'-[5-(1-hydroxyethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

To N-hydroxy-N'-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[(4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide (150mg, 0.36mmol), ethanol(20ml) and then sodium borohydride(17mg, 0.45mmol) were added slowly. The resulting mixture was stirred at 20℃ for 4 hours, concentrated under the reduced pressure to remove the solvent, and extracted with methylene chloride with addition of water. The organic layer was dried with magnesium sulfate and purified by column chromatography to obtain the titled compound.

yield : 75.6%

m.p. : 94~96℃

Example 139)

N-Hydroxy-N'-[5-(1-hydroxyethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-[5-(1-hydroxyethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 138 to obtain the titled compound.

yield : 65.6%

m.p. : 123~125℃

Example 140) N-Hydroxy-N'-[5-(1-hydroxyethyl)-2-methoxy-6-methyl-pyridin-3-yl]-(4-phenylpiperazin-1-yl)carboxyimidamide

Methyl N-[5-(1-hydroxyethyl)-2-methoxy-6-methylpyridin-3-yl]-(4-phenylpiperazin-1-yl)iminothiolate was reacted by the same way with the example 138 to obtain the titled compound.

yield : 72.3%

m.p. : 154~155℃

Example 141)

N-Hydroxy-N'-[5-(1-hydroxyethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-[5-(1-hydroxyethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(4-methylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 138 to obtain the titled compound.

yield : 62.1%

m.p. : 187~189℃

Example 142)

N-Hydroxy-N'-[5-(1-hydroxyethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-[5-(1-hydroxyethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 138 to obtain the titled compound.

yield : 63.8%

m.p. : 156~157℃

Example 143)

N-Hydroxy-N'-[5-(1-hydroxyethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(2-methylthiophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-[5-(1-hydroxyethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(2-methylthiophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 138 to obtain the titled compound.

yield : 70.2%

m.p. : 162~163℃

Example 144)

N-Hydroxy-N'-[5-(1-hydroxyiminoethyl)-2-methoxy-6-methyl-pyridin-3-yl]-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 23.2%

Example 145)

N-Hydroxy-N'-[5-(1-hydroxyiminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 35.6%

Example 146)

N-Hydroxy-N'-[5-(1-hydroxyiminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 33.3%

Example 147)

N-Hydroxy-N'-[5-(1-hydroxyiminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(2-methylthiophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methyl-thiophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 30.2%

Example 148)

N-Hydroxy-N'-[5-(1-hydroxyiminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dinitrophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dinitrophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 29.5%

Example 149)

N-Hydroxy-N'-[5-(1-hydroxyiminoethyl)-2-methoxy-6-me-thylpyridin-3-yl]-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-acetyl-2-methoxy-6-methylpyridin-3-yl)-[4-(4-

methylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 25.0%

Example 150)

N-Hydroxy-N'-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 45.6%

Example 151)

N-Hydroxy-N'-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 42.2%

Example 152)

N-Hydroxy-N'-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 53.1%

Example 153)

N-Hydroxy-N'-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(2-methylthiophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(2-methylthiophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 44.7%

Example 154)

N-Hydroxy-N'-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dinitrophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-dinitrophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 52.1%

Example 155)

N-Hydroxy-N'-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-chlorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-[5-(1-aminoethyl)-2-methoxy-6-methylpyridin-3-yl]-[4-(3,5-chlorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 47.6%

Example 156)

N-Hydroxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 71.2%

m.p. : 176~178℃

Example 157)

N-Hydroxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(2-ethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(2-ethylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 65.0%

m.p. : 182~184℃

Example 158)

N-Hydroxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 59.1%

m.p. : 152~155℃

Example 159)

N-Hydroxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 55.6%

m.p. : 156~157℃

Example 160)

N-Hydroxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 54.4%

m.p. : 158~160℃

Example 161)

N-Hydroxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 50.1%

m.p. : 168~170℃

Example 162)

N-Hydroxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-diethylisophthalate-1-yl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-diethylisophthal-1-yl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 57.3%

m.p. : 101~103℃

Example 163)

N-Hydroxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimid-amide

Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 45.0%

m.p. : 143~145℃

Example 164)

N-Hydroxy-N'-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 66.6%

m.p. : 170~172℃

Example 165)

N-Hydroxy-N'-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(2-ethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-ethyl-phenyl)piperazin-1-yl]iminothiolate was reacted by the same way with

the example 125 to obtain the titled compound.

yield : 60.4%

m.p. : 185~187℃

Example 166)

N-Hydroxy-N'-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 65.1%

m.p. : 75~77℃

Example 167)

N-Hydroxy-N'-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 61.2%

m.p. : 67~69℃

Example 168)

N-Hydroxy-N'-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 70.1%

m.p. : 75~77℃

Example 169)

N-Hydroxy-N'-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(2-

methylthiophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 67.2%

m.p. : 163~165℃

Example 170)

N-Hydroxy-N'-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-{4-[3,5-bis(hydroxymethyl)phenyl]piperazin-1-yl}carboxyimidamide

Methyl N-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-{4-[3,5-bis(hydroxymethyl)phenyl]piperazin-1-yl}iminothiolate was reacted by the same way with the example 125 to obtain the titled compound

yield : 59.4%

Example 171)

N-Hydroxy-N'-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 125 to obtain the titled compound.

yield : 48.7%

m.p. : 68~70℃

Example 172)

N-Hydroxy-N'-(2-methoxyquinolin-3-yl)-[4-(3,5-dimethoxyphenyl)-piperazin-1-yl]carboxyimidamide

Methyl N-(2-methoxyquinolin-3-yl)-[4-(3,5-dimethoxyphenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 41.0%

m.p. : 215~217℃

Example 173)

N-Hydroxy-N'-(2-methoxyquinolin-3-yl)-[4-(3,5-dimethylphenyl)-piperazin-1-yl]carboxyimidamide

Methyl N-(2-methoxyquinolin-3-yl)-[4-(3,5-dimethylphenyl)-

piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 44.2%

m.p. : 182~184℃

Example 174)

N-Hydroxy-N'-(2-methoxyquinolin-3-yl)-[4-(3,5-difluoro-phenyl)-piperazin-1-yl]carboxyimidamide

Methyl N-(2-methoxyquinolin-3-yl)-[4-(3,5-difluorophenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 38.1%

m.p. : 163~165℃

Example 175)

N-Hydroxy-N'-(2-methoxyquinolin-3-yl)-[4-(2-methoxyphenyl)-piperazin-1-yl]carboxyimidamide

Methyl N-(2-methoxyquinolin-3-yl)-[4-(2-methoxyphenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 43.2%

m.p. : 210~212℃

Example 176)

N-Hydroxy-N'-(2-methoxyquinolin-3-yl)-[4-(3-chlorophenyl)-piperazin-1-yl]carboxyimidamide

Methyl N-(2-methoxyquinolin-3-yl)-[4-(3-chlorophenyl)piperazin-1-yl]-iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 45.2%

m.p. : 162~164℃

Example 177)

N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-(4-phenyl-

piperazin-1-yl)carboxyimidamide

Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-(4-phenylpiperazin-1-yl)iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 62.7%

m.p. : 160~162℃

Example 178)

N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(4-methylphenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 60.1%

m.p. : 181~183℃

Example 179)

N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(2-ethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(2-ethylphenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 65.4%

m.p. : 194~196℃

Example 180) N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3,5-dimethylphenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 64.1%

m.p. : 184~186℃

Example 181) N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-

(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 65.5%

m.p. : 189~191℃

Example 182) N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3,5-difluorophenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 60.0%

m.p. : 179~181℃

Example 183)

N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3-chlorophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3-chlorophenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 58.7%

m.p. : 174~176℃

Example 184)

N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3-bromophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3-bromophenyl)-piperazin-1-yl]iminothiolate was reacted by the same way with the example 96 to obtain the titled compound.

yield : 61.2%

m.p. : 178~180℃

Example 185)

N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(2-methyl-

thiophenyl)piperazin-1-yl]carboxyimidamide

Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]iminothiolate was reacted by the same way with the ex-ample 96 to obtain the titled compound.

yield : 60.5%

m.p. : 194~196℃

Example 186) N-Methoxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-(4-phenylpiperazin-1-yl)carboxyimidamide

To N-hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-(4-phenylpiperazin-1-yl)carboxyimidamide (0.5g, 1.41mmol) dissolved in dimethylformamide (15ml), sodium hydride(60%, 57.8mg, 1.45mmol) and methyl iodide (0.20g, 1.41mmol) were added and stirred for 4 hours and then water(20ml) was added thereto to stop reaction. The resulting mixture was extracted with ethylether. The organic layer was concentrated under the reduced pressure to remove the solvent and purified by column chromatography to obtain the titled compound.

yield : 89.1%

Example 187)

N-Methoxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide

N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 92.2%

Example 188)

N-Methoxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 90.0%

Example 189)

N-Methoxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide

N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 92.2%

Example 190)

N-Methoxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide

N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 85.2%

Example 191)

N-Methoxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]carboxyimidamide

N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 89.2%

Example 192)

N-Methoxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dinitrophenyl)piperazin-1-yl]carboxyimidamide

N-Hydroxy-N'-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dinitrophenyl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 79.5%

Example 193)

N-Methoxy-N'-(5-ethyl-6-methyl-2-methoxypyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]carboxyimidamide

N-Hydroxy-N'-(5-ethyl-6-methyl-2-methoxypyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 84.2%

m.p. : 163~165℃

Example 194)

N-Methoxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimid-amide

N-Hydroxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 91.3%

Example 195)

N-Methoxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-diethylisophthal-1-yl)piperazin-1-yl]carboxyimidamide

N-Hydroxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-diethylisophthal-1-yl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 94.0%

Example 196)

N-Methoxy-N'-(6-ethyl-5-hydroxymethyl-2-methoxypyridin-3-yl)-{4-[3,5-bis(hydroxymethyl)phenyl-1-yl]piperazin-1-yl}carboxyimidamide

N-methoxy-N'-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-diethylisophthal-1-yl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 68.0%

Example 197)

N-Methoxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(4-methyl-phenyl)piperazin-1-yl]carboxyimidamide

N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(4-methylphenyl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 86.7%

Example 198) N-Methoxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide

N-Hydroxy-N'-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]carboxyimidamide was reacted by the same way with the example 186 to obtain the titled compound.

yield : 87.0%

Example 199) Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-(4-phenylpiperazin-1-yl)-iminothiolate

To 1-[(5,6-dimethyl-2-methoxypyridin-3-yl)aminocarbonyl]-4-phenylpiperazine (0.5g, 1.40mmol) dissolved in dimethylformamide(15ml), sodium hydride (60%, 56.1mg, 1.40mmol) and methyl iodide (0.20g, 1.41mmol) were added. The resulting mixture was stirred for 2 hours and then water(20ml) was added thereto to stop reaction. The resulting mixture was purified by column chromatography to obtain the titled compound.

yield : 92.4%

Example 200) Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(4-et-hylphenyl)-piperazin-1-yl]iminothiolate

1-[(5,6-Dimethyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(4-methylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 95.2%

Example 201) Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(4-n-butylphenyl)piperazin-1-yl]iminothiolate

1-[(5,6-Dimethyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(4-n-

butylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 93.4%

Example 202) Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethylphenyl)-piperazin-1-yl]iminothiolate

1-[(5,6-Dimethyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-dimethylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 97.2%

Example 203) Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(2-methoxyphenyl)-piperazin-1-yl]iminothiolate

1-[(5,6-Dimethyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(2-methoxyphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 97.4%

Example 204) Methyl N-(5.6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethoxyphenyl)-piperazin-1-yl]iminothiolate

1-[(5,6-Dimethyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 95.2%

Example 205) Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-di-fluorophenyl)-piperazin-1-yl]iminothiolate

1-[(5,6-Dimethyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-difluorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 90.1%

Example 206) Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-di-chlorophenyl)-piperazin-1-yl]iminothiolate

1-[(5,6-Dimethyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-dichlorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 92.5%

Example 207) Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3-bromophenyl)-piperazin-1-yl]iminothiolate

1-[(5,6-Dimethyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3-bromophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 89.5%

Example 208) Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-di-nitrophenyl)-piperazin-1-yl]iminothiolate

1-[(5,6-Dimethyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-dinitrophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 92.9%

Example 209) Methyl N-(5,6-dimethyl-2-methoxypyridin-3-yl)-[4-(3,5-di-ethylisophthal-1-yl)-piperazin-1-yl]iminothiolate

1-[(5,6-Dimethyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-diethylisophthal-1-yl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 92.9%

Example 210) Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-(4-phenyl)piperazin-1-yl]iminothiolate

1-[(5-Ethyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-

phenylpiperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 92.2%

Example 211) Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methoxyphenyl)piperazin-1-yl]iminothiolate

1-[(5-Ethyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(2-methoxyphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 87.2%

Example 212) Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)-piperazin-1-yl]iminothiolate

1-[(5-Ethyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 92.4%

Example 213) Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-ethylphenyl)piperazin-1-yl]iminothiolate

1-[(5-Ethyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(2-ethylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 93.6%

Example 214) Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate

1-[(5-Ethyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(3,5-dimethylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 96.2%

Example 215) Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)-piperazin-1-yl]iminothiolate

1-[(5-Ethyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(3,5-difluorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 92.5%

Example 216) Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dichlorophenyl)-piperazin-1-yl]iminothiolate

1-[(5-Ethyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(3,5-dichlorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 93.2%

Example 217) Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-phenylphenyl)piperazin-1-yl]iminothiolate

1-[(5-Ethyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(2-phenylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 91.4%

Example 218) Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dinitrophenyl)-piperazin-1-yl]iminothiolate

1-[(5-Ethyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(3,5-dinitrophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 94.2%

Example 219) Methyl N-(5-ethyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]iminothiolate

1-[(5-Ethyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(2-methylthiophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 90.5%

Example 220) Methyl

N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)amino-thiocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 93.2%

Example 221) Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)amino-thiocarbonyl]-4-(3,5-dimethylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 92.9%

Example 222) Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothio-carbonyl]-4-(3,5-difluorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 88.5%

Example 223) Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-methoxyphenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothio-carbonyl]-4-(2-methoxyphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 90.2%

Example 224) Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-(4-phenyl-piperazin-1-yl)iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothio-

carbonyl]-4-phenylpiperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 93.5%

Example 225) Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(4-methylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 97.5%

Example 226) Methyl N-(5-methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)-[4-(2-chlorophenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(2-chlorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 95.5%

Example 227) Methyl N-(2-methoxy-5-methylcarbonyl-6-methylpyridin- 3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(3,5-dimethylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 96.2%

Example 228) Methyl N-(2-methoxy-5-methylcarbonyl-6-methylpyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 95.4%

Example 229) Methyl N-(2-methoxy-5-methylcarbonyl-6-methylpyridin-3-yl)-(4-phenylpiperazin-1-yl)iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-phenylpiperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 90.1%

Example 230) Methyl N-(2-methoxy-5-methylcarbonyl-6-methylpyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(4-methylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 92.2%

Example 231) Methyl N-(2-methoxy-5-methylcarbonyl-6-methylpyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(3,5-difluorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 93.1%

Example 232) Methyl N-(2-methoxy-5-methylcarbonyl-6-methylpyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]iminothiolate

1-[(5-Methoxycarbonyl-2-methoxy-6-methylpyridin-3-yl)aminothiocarbonyl]-4-(2-methylthiophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 90.0%

Example 233) Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(4-methylphenyl)piperazin-1-yl]iminothiolate

1-[(6-Ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(4-methylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 91.1%

Example 234) Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(2-ethylphenyl)piperazin-1-yl]iminothiolate

1-[(6-Ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)aminothio-

carbonyl]-4-(2-ethylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 90.4%

Example 235) Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]iminothiolate

1-[(6-Ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-dimethylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 95.5%

Example 236) Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]iminothiolate

1-[(6-Ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 95.4%

Example 237) Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-dichlorophenyl)piperazin-1-yl]iminothiolate

1-[(6-Ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-dichlorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 90.5%

Example 238) Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(2-methylthiophenyl)piperazin-1-yl]iminothiolate

1-[(6-Ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(2-methylthiophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 92.0%

Example 239) Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-diethylisophthalate-1-yl)piperazin-1-yl]iminothi-olate

1-[(6-Ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-diethylisophthalate-1-yl)piperazine was reacted by the

same way with the example 199 to obtain the titled compound.

yield : 93.2%

Example 240) Methyl N-(6-ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate

1-[(6-Ethyl-5-methoxycarbonyl-2-methoxypyridin-3-yl)aminothiocarbonyl]-4-(3,5-difluorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 95.2%

Example 241) Methyl N-(2-methoxyquinolin-3-yl)-[4-(3,5-dimethoxyphe-nyl)piperazin-1-yl]-iminothiolate

1-[(2-Methoxyquinolin-3-yl)aminothiocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 90.3%

Example 242) Methyl N-(2-methoxyquinolin-3-yl)-[4-(3,5-dimethylphenyl)piperazin-1-yl]-iminothiolate

1-[(2-Methoxyquinolin-3-yl)aminothiocarbonyl]-4-(3,5-dimethylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 91.1%

Example 243) Methyl N-(2-methoxyquinolin-3-yl)-[4-(3,5-difluorophenyl)piperazin-1-yl]iminothiolate

1-[(2-Methoxyquinolin-3-yl)aminothiocarbonyl]-4-(3,5-difluorophenyl)-piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 94.2%

Example 244) Methyl N-(2-methoxyquinolin-3-yl)-[4-(2-methoxyphenyl)-piperazin-1-yl]iminothiolate

1-[(2-Methoxyquinolin-3-yl)aminothiocarbonyl]-4-(2-methoxyphenyl)-piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 92.4%

Example 245) Methyl N-(2-methoxyquinolin-3-yl)-[4-(3-chlorophenyl)pi-perazine-1-yl]-iminothiolate

1-[(2-Methoxyquinolin-3-yl)aminothiocarbonyl]-4-(3-chlorophenyl)-piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 90.3%

Example 246) Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-(4-phenyl-piperazin-1-yl)-iminothiolate

1-[(4,5-Dimethyl-2-methoxyphenyl-1-yl)aminothiocarbonyl]-4-phenyl-piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 95.4%

Example 247) Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(4-methylphenyl)-piperazin-1-yl]iminothiolate

1-[(4,5-Dimethyl-2-methoxyphenyl-1-yl)aminothiocarbonyl]-4-(4-methylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 94.4%

Example 248) Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(2-ethylphenyl)piperazin-1-yl]iminothiolate

1-[(4,5-Dimethyl-2-methoxyphenyl-1-yl)aminothiocarbonyl]-4-(2-ethylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 96.2%

Example 249) Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3,5-di-methylphenyl)-piperazin-1-yl]iminothiolate

1-[(4,5-Dimethyl-2-methoxyphenyl-1-yl)aminothiocarbonyl]-4-(3,5-dimethylphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 96.8%

Example 250) Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3,5-dimethoxy-phenyl)piperazin-1-yl]iminothiolate

1-[(4,5-Dimethyl-2-methoxyphenyl-1-yl)aminothiocarbonyl]-4-(3,5-dimethoxyphenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 95.7%

Example 251) Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3,5-difluorophenyl)-piperazin-1-yl]iminothiolate

1-[(4,5-Dimethyl-2-methoxyphenyl-1-yl)aminothiocarbonyl]-4-(3,5-difluorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 90.4%

Example 252) Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3-chlorophenyl)-piperazin-1-yl]iminothiolate

1-[(4,5-Dimethyl-2-methoxyphenyl-1-yl)aminothiocarbonyl]-4-(3-chlorophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 94.2%

Example 253) Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(3-bromophenyl)-piperazin-1-yl]iminothiolate

1-[(4,5-Dimethyl-2-methoxyphenyl-1-yl)aminothiocarbonyl]-4-(3-bromophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 94.4%

Example 254) Methyl N-(4,5-dimethyl-2-methoxyphenyl-1-yl)-[4-(2-methylthiophenyl)-piperazin-1-yl]iminothiolate

1-[(4,5-Dimethyl-2-methoxyphenyl-1-yl)aminothiocarbonyl]-4-(2-methylthiophenyl)piperazine was reacted by the same way with the example 199 to obtain the titled compound.

yield : 93.5%

Physical data of the compounds prepared in the above examples are as follows :

Example 1 ^{1}H NMR($CDCl_3$) : δ 2.37(3H,s), 2.39(3H,s), 3.27(4H,t), 3.74(4H,t), 3.97(3H,s), 6.97(2H,m), 7.31(2H,t)

Example 2 ^{1}H NMR($CDCl_3$) : δ 2.36(3H,s), 2.40(3H,s), 3.13(4H,t), 3.75(4H,t), 3.89(3H,s), 3.97(3H,s), 6.95(3H,m), 7.05(2H,m)

Example 3 ^{1}H NMR($CDCl_3$) : δ 2.37(3H,s), 2.39(3H,s), 3.25(4H,t), 3.71(4H,t), 3.79(6H,s), 3.97(3H,s), 6.10(3H,m)

Example 4 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 2.37(3H,s), 2.41(3H,s), 2.74(2H,q), 2.94(4H,t), 3.68(4H,t), 3.97(3H,s), 6.72(1H,brs), 7.08(2H,m), 7.19(1H,t), 7.25(1H,s)

Example 5 ^{1}H NMR($CDCl_3$) : δ 0.92(3H,t), 1.35(2H,m), 1.57(2H,m), 2.37(3H,s), 2.39(3H,s), 2.56(2H,t), 3.25(4H,t), 3.78(4H,t), 3.97(3H,s), 6.95(2H,brs), 7.14(2H,m)

Example 6 ^{1}H NMR($CDCl_3$) : δ 1.23(6H,d), 2.38(3H,s), 2.42(3H,s), 2.95(4H,t), 3.53(1H,m), 3.72(4H,t), 3.98(3H,s), 7.11(1H,m), 7.29(1H,m)

Example 7 ^{1}H NMR($CDCl_3$) : δ 2.30(6H,s), 2.37(3H,s), 2.40(3H,s), 3.25(4H,t), 3.75(4H,t), 3.97(3H,s), 6.62(3H,m)

Example 8 ^{1}H NMR($CDCl_3$) : δ 2.21(6H,s), 2.22(6H,s), 2.38(3H,s), 2.43(3H,s), 3.17(4H,t), 3.67(4H,t), 4.00(3H,s), 6.84(1H,s)

Example 9 ^{1}H NMR($CDCl_3$) : δ 2.37(3H,s), 2.40(3H,s), 3.14(4H,t), 3.73(4H,t), 3.98(3H,s), 6.99(2H,m), 7.07(2H,m)

Example 10 ^{1}H NMR($CDCl_3$) : δ 2.37(3H,s), 2.39(3H,s), 3.26(4H,t), 3.70(4H,t), 3.98(3H,s), 6.85(1H,m), 7.01(1H,d), 7.05(1H,s), 7.13(1H,t)

Example 11 ^{1}H NMR($CDCl_3$) : δ 2.37(3H,s), 2.39(3H,s), 3.27(4H,t), 3.69(4H,t), 3.98(3H,s), 6.75(2H,s), 6.84(1H,s)

Example 12 ^{1}H NMR($CDCl_3$) : δ 2.37(3H,s), 2.39(3H,s), 3.27(4H,t), 3.69(4H,t), 3.97(3H,s), 6.30(1H,t), 6.37(2H,d)

Example 13 ^{1}H NMR($CDCl_3$) : δ 2.38(3H,s), 2.40(3H,s), 3.31(4H,s), 3.73(4H,t), 3.98(3H,s), 7.09(1H,d), 7.13(2H,m), 7.38(1H,t)

Example 14 ^{1}H NMR($CDCl_3$) : δ 2.38(3H,s), 2.42(3H,s), 2.43(3H,s), 3.05(4H,t), 3.73(4H,t), 3.99(3H,s), 7.05(1H,brs), 7.13(1H,s)

Example 15 ^{1}H NMR($CDCl_3$) : δ 2.39(3H,s), 2.45(3H,s), 3.57(4H,t), 3.88(4H,t), 4.08(3H,s), 7.98(2H,s), 8.45(1H,s)

Example 16 ^{1}H NMR($CDCl_3$) : δ 2.38(3H,s), 2.40(3H,s), 3.26(4H,t), 3.70(4H,t), 3.98(3H,s), 6.35(1H,s), 6.42(2H,s)

Example 17 ^{1}H NMR($CDCl_3$) : δ 2.38(3H,s), 2.40(3H,s), 2.54(3H,s), 3.46(4H,t), 3.74(4H,t), 3.99(3H,s), 6.88(2H,d), 7.90(2H,d)

Example 18 ^{1}H NMR($CDCl_3$) : δ 2.39(3H,s), 2.40(3H,s), 2.91(4H,t), 3.22(3H,s), 3.46(4H,t), 3.85(3H,s), 3.95(3H,s), 6.89(3H,m), 7.02(1H,m)

Example 19 ^{1}H NMR($CDCl_3$) : δ 2.39(3H,s), 2.40(3H,s), 3.01(4H,t), 3.21(3H,s), 3.40(4H,t), 3.75(6H,s), 3.92(3H,s), 6.03(3H,s)

Example 20 ^{1}H NMR($CDCl_3$) : δ 2.26(6H,s), 2.39(3H,s), 2.40(3H,s), 2.99(4H,t), 3.22(3H,s), 3.40(4H,t), 3.93(3H,s), 6.52(3H,m)

Example 21 ^{1}H NMR($CDCl_3$) : δ 2.40(3H,s), 2.41(3H,s), 3.03(4H,t), 3.21(3H,s), 3.38(4H,t), 3.93(3H,s), 6.68(2H,s), 6.81(1H,s)

Example 22 ^{1}H NMR($CDCl_3$) : δ 2.40(3H,s), 2.41(3H,s), 3.03(4H,t), 3.21(3H,s), 3.39(4H,t), 3.93(3H,s), 6.27(3H,m)

Example 23 ^{1}H NMR($CDCl_3$) : δ 2.40(9H,s), 2.87(4H,t), 3.22(3H,s),

3.46(4H,t), 3.96(3H,s), 7.02(1H,brs), 7.11(3H,s)

Example 24 ^{1}H NMR($CDCl_3$) : δ 2.43(6H,s), 3.24(3H,s), 3.27(4H,t), 3.45(4H,t), 3.95(3H,s), 7.89(2H,d), 8.40(1H,s)

Example 25 ^{1}H NMR($CDCl_3$) : δ 2.38(3H,s), 2.39(3H,s), 2.95(4H,t), 3.21(3H,s), 3.37(4H,t), 3.92(3H,s), 5.62(1H,s), 5.65(2H,s)

Example 26 ^{1}H NMR($CDCl_3$) : δ 1.65(3H,t), 2.39(3H,s), 2.40(3H,s), 2.96(4H,t), 3.35(4H,t), 3.74(2H,q), 3.75(6H,s), 3.92(3H,s), 6.02(3H,s)

Example 27 ^{1}H NMR($CDCl_3$) : δ 1.17(3H,t), 2.25(6H,s), 2.39(3H,s), 2.40(3H,s), 2.95(4H,t), 3.36(4H,t), 3.74(2H,q), 3.92(3H,s), 6.50(3H,m)

Example 28 ^{1}H NMR($CDCl_3$) : δ 2.32(3H,s), 2.34(3H,s), 3.34(4H,t), 3.78(6H,s), 3.98(3H,s), 4.07(4H,t), 6.12(3H,m)

Example 29 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 2.35(3H,s), 2.37(3H,s), 2.74(2H,q), 3.02(4H,t), 3.97(3H,s), 4.02(4H,t), 7.09(2H,q), 7.19(1H,t), 7.55(1H,s)

Example 30 ^{1}H NMR($CDCl_3$) : δ 2.29(6H,s), 2.32(3H,s), 2.35(3H,s), 3.31(4H,t), 3.98(3H,s), 4.04(4H,t), 6.59(3H,brs)

Example 31 ^{1}H NMR($CDCl_3$) : δ 2.32(3H,s), 2.35(3H,s), 3.33(4H,t), 3.98(3H,s), 4.06(4H,t), 6.82(1H,d), 7.01(2H,m), 7.13(1H,t)

Example 32 ^{1}H NMR($CDCl_3$) : δ 2.44(3H,s), 2.49(3H,s), 3.48(4H,t), 4.05(3H,s), 4.25(4H,t), 6.98(3H,m)

Example 33 ^{1}H NMR($CDCl_3$) : δ 2.35(3H,s), 2.36(3H,s), 2.43(3H,s), 3.12(4H,t), 3.97(3H,s), 4.05(4H,t), 6.87(1H,d), 7.05(1H,brs), 7.13(2H,m)

Example 34 ^{1}H NMR($CDCl_3$) : δ 1.26(6H,m), 2.30(6H,s), 2.70(2H,t), 2.78(2H,t), 3.25(4H,t), 3.74(4H,t), 3.99(3H,s), 6.65(3H,m)

Example 35 ^{1}H NMR($CDCl_3$) : δ 1.24(6H,m), 2.69(2H,t), 2.78(2H,t), 3.24(4H,t), 3.71(4H,t), 3.78(6H,s), 3.98(3H,s), 6.07(1H,s), 6.11(2H,brs)

Example 36 ^{1}H NMR($CDCl_3$) : δ 3.34(4H,t), 3.88(4H,t), 4.15(3H,s), 7.05(3H,m), 7.35(3H,m), 7.43(2H,m), 7.70(1H,brs)

Example 37 ^{1}H NMR($CDCl_3$) : δ 3.17(4H,t), 3.83(4H,t), 3.90(3H,s), 4.16(3H,s), 6.99(4H,m), 7.49(2H,m), 7.75(2H,m)

Example 38 ^{1}H NMR($CDCl_3$) : δ 3.22(4H,t), 3.30(4H,t), 3.79(6H,s),

4.11(3H,s), 7.20(1H,d), 7.33(2H,m), 7.50(2H,m), 7.62(1H,d), 7.76(1H,m), 7.83(1H,m)

Example 39 ^{1}H NMR($CDCl_3$) : δ 1.28(3H,t), 2.78(2H,q), 3.02(4H,t), 3.89(4H,t), 4.15(3H,s), 7.13(2H,m), 7.21(1H,t), 7.28(1H,m), 7.43(3H,m), 7.70(1H,d)

Example 40 ^{1}H NMR($CDCl_3$) : δ 1.24(6H,d), 2.98(4H,t), 3.56(1H,m), 3.82(4H,t), 4.15(3H,s), 7.16(3H,m), 7.30(1H,d), 7.43(2H,brs), 7.69(2H,d)

Example 41 ^{1}H NMR($CDCl_3$) : δ 0.93(3H,t), 1.35(2H,m), 1.57(2H,m), 2.56(2H,t), 3.35(4H,t), 3.88(4H,t), 4.15(3H,s), 7.19(3H,brs), 7.43(3H,brs), 7.70(2H,brs)

Example 42 ^{1}H NMR($CDCl_3$) : δ 2.30(6H,s), 3.26(4H,t), 3.78(4H,t), 4.14(3H,s), 6.60(3H,s), 7.30(2H,m), 7.50(1H,s), 7.55(1H,m)

Example 43 ^{1}H NMR($CDCl_3$) : δ 2.21(6H,s), 2.34(6H,s), 3.20(4H,t), 3.83(4H,t), 4.17(3H,s), 6.85(1H,s), 7.46(2H,m), 7.61(1H,brs), 7.72(1H,d)

Example 44 ^{1}H NMR($CDCl_3$) : δ 3.20(4H,t), 3.91(4H,t), 4.15(3H,s), 7.07(4H,m), 7.42(3H,m), 7.70(1H,d)

Example 45 ^{1}H NMR($CDCl_3$) : δ 3.30(4H,t), 3.90(4H,t), 4.16(3H,s), 6.95(1H,d), 7.05(1H,d), 7.15(2H,m), 7.42(2H,m), 7.53(1H,s), 7.69(1H,d)

Example 46 ^{1}H NMR($CDCl_3$) : δ 3.27(4H,t), 3.78(4H,t), 4.16(3H,s), 6.39(3H,m), 7.52(2H,m), 7.74(2H,m)

Example 47 ^{1}H NMR($CDCl_3$) : δ 3.34(4H,t), 3.90(4H,t), 4.16(3H,s), 7.15(3H,m), 7.40(3H,m), 7.52(1H,brs), 7.70(1H,d)

Example 48 ^{1}H NMR($CDCl_3$) : δ 3.55(4H,t), 3.98(4H,t), 4.19(3H,s), 7.46(3H,m), 7.73(1H,m), 8.00(2H,s), 8.44(1H,s)

Example 49 ^{1}H NMR($CDCl_3$) : δ 3.25(4H,t), 3.73(4H,t), 4.13(3H,s), 5.68(1H,brs), 5.79(2H,brs), 7.49(2H,m), 7.74(2H,m)

Example 50 ^{1}H NMR($CDCl_3$) : δ 2.54(3H,s), 3.49(4H,t), 3.92(4H,t), 4.16(3H,s), 6.95(2H,d), 7.43(2H,m), 7.51(1H,brs), 7.71(1H,d), 7.92(2H,d)

Example 51 ^{1}H NMR($CDCl_3$) : δ 2.47(3H,s), 3.30(4H,t), 4.04(4H,t), 4.19(3H,s), 7.20(3H,brs), 7.47(2H,m), 7.60(2H,m), 7.76(1H,m)

Example 52 ^{1}H NMR($CDCl_3$) : δ 2.92(4H,t), 3.57(4H,t), 4.11(3H,s),

7.15(1H,d), 7.12(1H,t), 7.30(4H,m), 7.41(4H,m), 7.54(1H,m), 7.64(3H,m)

Example 53 ^{1}H NMR($CDCl_3$) : δ 3.19(4H,t), 3.38(3H,s), 3.68(4H,t), 3.78(6H,s), 4.07(3H,s), 6.09(3H,brm), 7.50(2H,m), 7.80(2H,m)

Example 54 ^{1}H NMR($CDCl_3$) : δ 3.08(4H,t), 3.39(3H,s), 3.73(4H,t), 3.88(3H,s), 4.09(3H,s), 6.92(4H,m), 7.50(2H,m), 7.80(2H,m)

Example 55 ^{1}H NMR($CDCl_3$) : δ 2.30(6H,s), 3.19(4H,t), 3.39(3H,s), 3.70(4H,t), 4.08(3H,s), 6.59(3H,brs), 7.52(2H,s), 7.80(2H,m)

Example 56 ^{1}H NMR($CDCl_3$) : δ 3.20(4H,t), 3.39(3H,s), 3.66(4H,t), 4.07(3H,s), 6.35(3H,m), 7.52(2H,m), 7.82(2H,m)

Example 57 ^{1}H NMR($CDCl_3$) : δ 3.41(3H,s), 3.43(4H,t), 3.71(4H,t), 4.09(3H,s), 7.55(2H,m), 7.79(1H,m), 7.88(1H,m), 7.96(2H,s), 8.44(1H,s)

Example 58 ^{1}H NMR($CDCl_3$) : δ 3.13(4H,t), 3.37(3H,s), 3.65(4H,t), 3.94(3H,s), 5.59(2H,m), 5.61(1H,s), 7.50(2H,m), 7.77(1H,m), 7.82(1H,m)

Example 59 ^{1}H NMR($CDCl_3$) : δ 1.33(3H,t), 3.15(4H,t), 3.65(4H,t), 3.77(6H,s), 3.91(2H,q), 4.08(3H,s), 6.09(3H,brs), 7.52(2H,m), 7.80(2H,m)

Example 60 ^{1}H NMR($CDCl_3$) : δ 1.34(3H,t), 2.28(6H,s), 3.12(4H,t), 3.62(4H,t), 3.91(2H,q), 4.08(3H,s), 6.55(3H,brs), 7.51(2H,m), 7.80(2H,m)

Example 61 ^{1}H NMR($CDCl_3$) : δ 1.33(3H,t), 3.15(4H,t), 3.61(4H,t), 3.91(2H,q), 4.08(3H,s), 6.77(2H,s), 6.87(1H,s), 7.53(2H,m), 7.78(1H,m), 7.85(1H,m)

Example 62 ^{1}H NMR($CDCl_3$) : δ 1.43(6H,d), 2.98(4H,t), 3.48(4H,d), 3.74(6H,s), 4.06(3H,s), 4.71(1H,m), 5.99(2H,s), 6.01(1H,s), 7.53(2H,m), 7.77(1H,m), 7.84(1H,m)

Example 63 ^{1}H NMR($CDCl_3$) : δ 3.49(4H,t), 3.96(3H,s), 4.15(3H,s), 4.31(4H,t), 7.06(3H,m), 7.44(3H,m), 7.71(2H,d)

Example 64 ^{1}H NMR($CDCl_3$) : δ 3.40(4H,t), 3.80(6H,s), 4.15(3H,s), 4.30(4H,t), 6.16(3H,brs), 6.84(1H,d), 7.23(1H,t), 7.44(2H,brs), 7.70(1H,brs)

Example 65 ^{1}H NMR($CDCl_3$) : δ 1.27(3H,t), 2.76(2H,q), 3.05(4H,t), 4.15(3H,s), 4.39(4H,t), 7.10(2H,m), 7.19(1H,s), 7.40(3H,m), 7.75(1H,m), 8.01(1H,s)

Example 66 ^{1}H NMR($CDCl_3$) : δ 2.31(6H,s), 3.36(4H,t), 4.14(3H,s),

4.38(4H,t), 6.64(3H,brs), 7.45(2H,m), 7.72(2H,m)

Example 67 ^{1}H NMR($CDCl_3$) : δ 3.34(4H,t), 4.16(3H,s), 4.38(4H,t), 6.85(1H,d), 7.01(1H,d), 7.06(1H,s), 7.15(1H,m), 7.42(3H,m), 7.68(1H,brs)

Example 68 ^{1}H NMR($CDCl_3$) : δ 3.42(4H,t), 4.16(3H,s), 4.30(4H,t), 6.39(3H,m), 7.20(1H,t), 7.43(1H,m), 7.69(2H,m)

Example 69 ^{1}H NMR($CDCl_3$) : δ 2.46(3H,s), 3.20(4H,t), 4.15(3H,s), 4.30(4H,t), 6.90(1H,m), 7.15(3H,m), 7.45(1H,m), 7.65(1H,t), 7.73(1H,m), 8.01(1H,d)

Example 70 ^{1}H NMR($CDCl_3$) : δ 2.56(3H,s), 3.60(4H,t), 4.15(3H,s), 4.30(4H,t), 6.96(2H,d), 7.44(1H,m), 7.59(1H,m), 7.74(2H,m), 7.95(2H,m)

Example 71 ^{1}H NMR($CDCl_3$) : δ 0.92(3H,t), 1.35(2H,m), 1.57(2H,m), 2.56(2H,t), 3.34(4H,t), 4.11(4H,t), 4.19(3H,s), 6.91(2H,m), 7.14(2H,m), 7.60(1H,t), 7.68(1H,t), 7.98(1H,d), 8.02(1H,d)

Example 72 ^{1}H NMR($CDCl_3$) : δ 1.52(3H,t), 3.32(4H,t), 3.79(6H,s), 3.80(4H,t), 4.60(2H,q), 6.14(3H,m), 7.44(2H,brs), 7.69(2H,brs)

Example 73 ^{1}H NMR($CDCl_3$) : δ 1.50(3H,t), 3.26(4H,t), 3.86(4H,t), 4.11(2H,q), 4.62(2H,q), 6.95(2H,m), 7.07(1H,brs), 7.55(3H,m), 7.80(2H,m)

Example 74 ^{1}H NMR($CDCl_3$) : δ 1.52(3H,t), 2.30(6H,s), 3.30(4H,t), 3.80(4H,t), 4.61(2H,q), 6.62(3H,brs), 7.48(2H,m), 7.76(2H,m)

Example 75 ^{1}H NMR($CDCl_3$) : δ 1.52(3H,t), 2.27(3H,s), 2.29(3H,s), 2.98(4H,t), 3.78(4H,t), 4.60(2H,q), 6.94(2H,m), 7.10(1H,m), 7.30(1H,brs), 7.47(2H,brs), 7.74(1H,brs)

Example 76 ^{1}H NMR($CDCl_3$) : δ 1.28(3H,t), 1.52(3H,t), 2.79(2H,q), 3.06(4H,t), 3.89(4H,t), 4.61(2H,q), 7.14(2H,m), 7.22(1H,t), 7.28(1H,d), 7.44(2H,m), 7.69(2H,m)

Example 77 ^{1}H NMR($CDCl_3$) : δ 1.54(3H,t), 3.36(4H,t), 3.91(4H,t), 4.63(2H,q), 6.88(2H,s), 6.90(1H,s), 7.47(2H,m), 7.59(1H,brs), 7.71(1H,m)

Example 78 ^{1}H NMR($CDCl_3$) : δ 1.52(3H,t), 3.30(4H,t), 3.83(4H,t), 4.60(2H,q), 6.90(1H,d), 7.03(1H,d), 7.10(1H,s), 7.15(1H,t), 7.43(2H,brs), 7.69(1H,brs)

Example 79 ^{1}H NMR($CDCl_3$) : δ 1.52(3H,t), 3.33(4H,t), 3.77(4H,t),

3.78(4H,t), 4.68(2H,q), 6.31(1H,t), 6.40(2H,d), 7.47(2H,m), 7.54(1H,m), 7.72(1H,t)

Example 80 ^{1}H NMR($CDCl_3$) : δ 1.52(3H,t), 2.44(3H,s), 3.13(4H,t), 3.89(4H,t), 4.61(2H,q), 7.15(4H,brs), 7.45(2H,m), 7.69(2H,brm)

Example 81 ^{1}H NMR($CDCl_3$) : δ 1.44(3H,t), 3.22(4H,t), 3.38(3H,s), 3.71(4H,t), 3.78(6H,s), 4.53(2H,q), 6.09(1H,brs), 6.13(2H,brs), 7.50(2H,m), 7.75(1H,m), 7.82(1H,m)

Example 82 ^{1}H NMR($CDCl_3$) : δ 1.43(3H,t), 3.22(4H,t), 3.38(3H,s), 3.66(4H,t), 4.54(2H,q), 6.76(2H,s), 6.86(1H,s), 7.51(2H,m), 7.76(1H,m), 7.83(1H,m)

Example 83 ^{1}H NMR($CDCl_3$) : δ 1.34(3H,t), 1.44(3H,t), 3.15(4H,t), 3.62(4H,t), 3.77(6H,s), 3.91(2H,q), 4.53(2H,q), 6.06(3H,brs), 7.51(2H,m), 7.75(1H,m), 7.81(1H,m)

Example 84 ^{1}H NMR($CDCl_3$) : δ 1.33(3H,t), 1.44(3H,t), 3.16(4H,t), 3.59(4H,t), 3.91(2H,q), 4.54(2H,q), 6.74(2H,s), 6.85(1H,s), 7.52(2H,m), 7.76(1H,m), 7.82(1H,m)

Example 85 ^{1}H NMR($CDCl_3$) : δ 1.34(3H,t), 1.45(3H,t), 2.28(6H,s), 3.15(4H,t), 3.63(4H,t), 3.91(2H,q), 4.53(2H,q), 6.56(3H,brs), 7.50(2H,m), 7.75(1H,d), 7.82(1H,d)

Example 86 ^{1}H NMR($CDCl_3$) : δ 2.30(6H,s), 3.27(4H,t), 3.73(4H,t), 4.03(3H,s), 6.60(3H,brs), 7.13(1H,s), 7.33(2H,t), 7.45(1H,s), 7.67(1H,m), 7.75(1H,m)

Example 87 ^{1}H NMR($CDCl_3$) : δ 3.20(4H,t), 3.40(4H,t), 3.75(6H,s), 3.99(3H,s), 6.10(3H,brs), 7.12(1H,s), 7.31(2H,t), 7.44(1H,s), 7.65(1H,m), 7.70(1H,m)

Example 88 ^{1}H NMR($CDCl_3$) : δ 3.32(4H,t), 3.73(4H,t), 4.03(3H,s), 6.32(1H,t), 6.41(2H,d), 7.13(1H,s), 7.34(2H,t), 7.43(1H,s), 7.67(1H,m), 7.75(1H,m)

Example 89 ^{1}H NMR($CDCl_3$) : δ 3.34(4H,t), 3.77(4H,t), 4.03(3H,s), 6.84(1H,m), 6.92(2H,m), 7.13(1H,s), 7.34(2H,m), 7.43(1H,s), 7.68(1H,m), 7.75(1H,m)

Example 90 ^{1}H NMR($CDCl_3$) : δ 2.20(6H,s), 2.85(4H,t), 3.18(3H,s), 3.32(4H,t), 3.99(3H,s), 6.39(2H,s), 6.47(1H,s), 7.20(1H,s), 7.35(1H,t), 7.43(1H,t), 7.53(1H,s), 7.69(1H,d), 7.73(1H,d)

Example 91 ^{1}H NMR($CDCl_3$) : δ 2.91(4H,t), 3.18(3H,s), 3.33(4H,t), 4.00(3H,s), 6.24(3H,brm), 7.21(1H,s), 7.37(1H,t), 7.45(1H,t), 7.53(1H,s), 7.70(1H,d), 7.74(1H,d)

Example 92 ^{1}H NMR($CDCl_3$) : δ 3.03(4H,t), 3.18(3H,s), 3.52(4H,t), 4.01(3H,s), 6.82(3H,brm), 7.12(1H,brs), 7.37(1H,m), 7.46(1H,m), 7.56(1H,m), 7.72(2H,m)

Example 93 ^{1}H NMR($CDCl_3$) : δ 2.88(4H,t), 3.18(3H,s), 3.33(4H,t), 3.71(6H,s), 3.99(3H,s), 5.92(2H,brs), 5.97(1H,brs), 7.20(1H,s), 7.36(1H,t), 7.43(1H,t), 7.52(1H,s), 7.69(1H,d), 7.73(1H,d)

Example 94 ^{1}H NMR($CDCl_3$) : δ 1.34(3H,t), 2.21(6H,s), 2.88(4H,t), 3.32(4H,t), 3.91(2H,q), 3.99(3H,s), 6.39(2H,s), 6.47(1H,s), 7.20(1H,s), 7.35(1H,t), 7.46(1H,t), 7.56(1H,s), 7.71(1H,d), 7.73(1H,d)

Example 95 ^{1}H NMR($CDCl_3$) : δ 1.35(3H,t), 2.90(4H,t), 3.33(4H,t), 3.70(6H,s), 3.92(2H,q), 3.99(3H,s), 5.92(2H,brs), 5.97(1H,brs), 7.25(1H,s), 7.36(1H,t), 7.43(1H,t), 7.52(1H,s), 7.72(1H,d), 7.73(1H,d)

Example 96 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.33(3H,s), 3.19(4H,s), 3.20(4H,s), 3.98(3H,s), 6.84(1H,s), 6.87(1H,t), 6.93(2H,d), 7.25(1H,d), 7.55(1H,s)

Example 97 ^{1}H NMR($CDCl_3$) : δ 2.13(3H,s), 2.27(3H,s), 2.32(3H,s), 3.13(4H,d), 3.19(4H,d), 3.98(3H,s), 6.81(1H,s), 6.83(2H,d), 7.07(2H,d), 7.54(1H,s)

Example 98 ^{1}H NMR($CDCl_3$) : δ 0.91(3H,t), 1.30(2H,m), 1.54(2H,m), 2.13(3H,s), 2.32(3H,s), 2.53(2H,t), 3.14(4H,d), 3.19(4H,d), 3.98(3H,s), 6.80(1H,s), 6.85(2H,d), 7.08(2H,d), 7.55(1H,s)

Example 99 ^{1}H NMR($CDCl_3$) : δ 2.13(3H,s), 2.27(6H,s), 2.32(3H,s), 3.12(4H,s), 3.13(4H,s), 3.89(3H,s), 6.56(3H,s), 6.81(1H,s), 7.54(1H,s)

Example 100 ^{1}H NMR($CDCl_3$) : δ 2.16(3H,s), 2.33(3H,s), 3.08(4H,t), 3.25(4H,t), 3.85(3H,s), 3.98(3H,s), 6.87(1H,t), 6.93(2H,d), 7.02(1H,m),

7.57(1H,s)

Example 101 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.32(3H,s), 3.17(8H,s), 3.77(6H,s), 3.98(3H,s), 6.04(1H,s), 6.08(2H,s), 6.81(1H,s), 7.53(1H,s)

Example 102 ^{1}H NMR($CDCl_3$) : δ 2.15(3H,s), 2.33(3H,s), 3.17(8H,s), 3.98(3H,s), 6.28(1H,t), 6.35(2H,d), 6.78(1H,s), 7.50(1H,s)

Example 103 H NMR($CDCl_3$) : δ 2.16(3H,s), 2.39(3H,s), 3.18(4H,s), 3.20(4H,s), 3.98(3H,s), 6.69(3H,s), 6.78(1H,s), 7.45(1H,s)

Example 104 ^{1}H NMR($CDCl_3$) : δ 2.15(3H,s), 2.33(3H,s), 3.18(8H,s), 3.98(3H,s), 6.78(1H,s), 6.82(1H,d), 6.97(1H,d), 7.03(1H,s), 7.11(1H,t), 7.51(1H,s)

Example 105 ^{1}H NMR($CDCl_3$) : δ 2.16(3H,s), 2.34(3H,s), 3.20(4H,s), 3.37(4H,s), 3.90(3H,s), 6.78(1H,s), 7.47(1H,s), 7.97(2H,s), 8.42(1H,s)

Example 106 ^{1}H NMR($CDCl_3$) : δ 1.40(6H,t), 2.17(3H,s), 2.30(3H,s), 3.29(4H,s), 3.33(4H,s), 3.98(3H,s), 4.38(4H,q), 7.41(1H,s), 7.72(2H,s), 8.16(1H,s)

Example 107 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.33(3H,s), 3.21(8H,s), 3.98(3H,s), 4.66(4H,s), 6.82(1H,s), 6.88(3H,s), 7.52(1H,s)

Example 108 ^{1}H NMR($CDCl_3$) : δ 1.19(3H,t), 2.36(3H,s), 2.52(2H,q), 3.07(4H,s), 3.30(4H,s), 3.84(3H,s), 3.97(3H,s), 6.85~7.03 (5H,m), 7.51(1H,s)

Example 109 ^{1}H NMR($CDCl_3$) : δ 1.14(3H,t), 2.36(3H,s), 2.50(2H,q), 3.17(8H,d), 3.77(6H,s), 3.98(3H,s), 6.04(1H,s), 6.07(2H,s), 6.80(1H,s), 7.56(1H,s)

Example 110 ^{1}H NMR($CDCl_3$) : δ 1.22(6H,m), 2.36(3H,s), 2.54(2H,q), 2.68(2H,q), 2.90(4H,s), 3.20(4H,s), 3.98(3H,s), 6.80(1H,s), 7.08(2H,m), 7.17(1H,t), 7.22(1H,d), 7.62(1H,s)

Example 111 ^{1}H NMR($CDCl_3$) : δ 1.14(3H,t), 2.36(3H,s), 2.50(2H,q), 3.18(4H,s), 3.25(4H,s), 3.98(3H,s), 6.89(4H,m), 7.27(2H,m), 7.52(1H,s)

Example 112 ^{1}H NMR($CDCl_3$) : δ 1.20(3H,t), 2.36(3H,s), 2.38(3H,s), 2.54(2H,q), 3.00(4H,s), 3.27(4H,s), 3.97(3H,s), 7.00(1H,brs) 7.01(1H,s), 7.10(3H,s), 7.55(1H,s)

Example 113 ^{1}H NMR($CDCl_3$) : δ 1.14(3H,t), 2.27(6H,s), 2.36(3H,s),

2.49(2H,q), 3.17(4H,s), 3.18(4H,s), 3.98(3H,s), 6.55(3H,s), 6.81(1H,s), 7.57(1H,s)

Example 114 ^{1}H NMR($CDCl_3$) : δ 1.15(3H,t), 2.36(3H,s), 2.50(2H,q), 3.17(8H,s), 3.98(3H,s), 6.28(1H,t), 6.35(2H,d), 6.65(1H,brs), 6.78(1H,s), 7.52(1H,s)

Example 115 ^{1}H NMR($CDCl_3$) : δ 1.15(3H,t), 2.36(3H,s), 2.50(2H,q), 3.17(8H,s), 3.98(3H,s), 6.17(1H,brs), 6.74(3H,m), 6.82(1H,s), 7.51(1H,s)

Example 116 ^{1}H NMR($CDCl_3$) : δ 1.15(3H,t), 2.32(3H,s), 2.48(2H,q), 2.84(4H,s), 2.94(4H,s), 3.94(3H,s), 6.73(1H,s), 7.00(1H,s), 7.09(1H,t), 7.24(2H,m), 7.29(1H,t), 7.35(2H,t), 7.51(1H,s), 7.58(2H,d)

Example 117 ^{1}H NMR($CDCl_3$) : δ 1.15(3H,t), 2.37(3H,s), 2.51(2H,q), 3.28(4H,s), 3.39(4H,s), 3.98(3H,s), 6.84(1H,brs), 7.47(1H,s), 7.96(2H,s), 8.42(1H,s)

Example 118 ^{1}H NMR($CDCl_3$) : δ 2.69(3H,s), 3.20(8H,s), 3.77(6H,s), 3.80(3H,s), 4.06(3H,s), 6.04(1H,s), 6.09(2H,s), 6.93(1H,s), 8.39(1H,s)

Example 119 ^{1}H NMR($CDCl_3$) : δ 2.28(6H,s), 2.70(3H,s), 3.20(8H,s), 3.80(3H,s), 4.06(3H,s), 6.56(3H,s), 6.94(1H,s), 8.40(1H,s)

Example 120 ^{1}H NMR($CDCl_3$) : δ 2.69(3H,s), 3.19(4H,d), 3.22(4H,d), 3.80(3H,s), 4.07(3H,s), 6.29(1H,t), 6.36(2H,d), 6.75(1H,brs), 6.93(1H,s), 8.36(1H,s)

Example 121 ^{1}H NMR($CDCl_3$) : δ 2.70(3H,s), 3.13(4H,s), 3.28(4H,s), 3.83(3H,s), 3.86(3H,s), 4.06(3H,s), 6.94(5H,m), 8.42(1H,s)

Example 122 ^{1}H NMR($CDCl_3$) : δ 2.70(3H,s), 3.23(8H,s), 3.78(3H,s), 4.07(3H,s), 6.89(1H,t), 6.94(2H,d), 6.99(1H,brs), 7.27(2H,d), 8.38(1H,s)

Example 123 ^{1}H NMR($CDCl_3$) : δ 2.27(3H,s), 2.69(3H,s), 3.17(4H,d), 3.22(4H,d), 3.78(3H,s), 4.06(3H,s), 6.84(2H,d), 6.98(1H,brs), 7.09(1H,d), 8.38(1H,s)

Example 124 ^{1}H NMR($CDCl_3$) : δ 2.70(3H,s), 3.22(8H,s), 3.80(3H,s), 4.06(3H,s), 6.78(1H,d), 6.84(1H,d), 6.88(1H,s), 6.98(1H,brs), 7.17(1H,t), 8.35(1H,s)

Example 125 ^{1}H NMR($CDCl_3$) : δ 2.39(3H,s), 3.17(8H,s), 3.76(6H,s),

4.00(3H,s), 4.59(2H,s), 6.03(1H,s), 6.07(2H,d), 6.88(1H,s), 7.79(1H,s)

Example 126 ^{1}H NMR($CDCl_3$) : δ 2.27(6H,s), 2.40(3H,s), 3.18(8H,s), 4.01(3H,s), 4.59(2H,s), 6.55(3H,s), 6.87(1H,s), 7.80(2H,s)

Example 127 ^{1}H NMR($CDCl_3$) : δ 2.40(3H,s), 3.19(8H,s), 4.00(3H,s), 4.61(2H,s), 6.27(1H,t), 6.35(2H,d), 6.86(1H,s), 7.79(1H,s)

Example 128 ^{1}H NMR($CDCl_3$) : δ 2.40(3H,s), 3.08(4H,s), 3.31(4H,s), 3.84(3H,s), 3.99(3H,s), 4.61(2H,s), 6.92(5H,m), 7.77(1H,s)

Example 129 ^{1}H NMR($CDCl_3$) : δ 2.39(3H,s), 3.20(8H,d), 4.00(3H,s), 4.58(2H,s), 6.90(4H,m), 7.27(2H,d), 7.79(1H,s)

Example 130 ^{1}H NMR($CDCl_3$) : δ 2.17(3H,s), 2.39(3H,s), 3.13(4H,d), 3.22(4H,d), 3.99(3H,s), 4.58(2H,s), 6.82(2H,d), 7.00(1H,brs), 7.06(2H,d), 7.78(1H,s)

Example 131 ^{1}H NMR($CDCl_3$) : δ 2.39(3H,s), 3.19(8H,d), 4.00(3H,s), 4.60(2H,s), 6.76(1H,d), 6.82(1H,d), 6.85(1H,s), 6.95(1H,brs), 7.16(1H,t), 7.77(1H,s)

Example 132 ^{1}H NMR($CDCl_3$) : δ 2.27(6H,s), 2.50(3H,s), 2.64(3H,s), 3.19(8H,d), 4.07(3H,s), 6.55(2H,s), 6.56(1H,s), 6.88(1H,s), 7.39(1H,brs), 8.19(1H,s)

Example 133 ^{1}H NMR($CDCl_3$) : δ 2.50(3H,s), 2.64(3H,s), 3.16(4H,s), 3.25(4H,s), 3.76(6H,s), 4.06(3H,s), 6.05(1H,s), 6.07(2H,s), 7.05(1H,brs), 8.13(1H,s)

Example 134 ^{1}H NMR($CDCl_3$) : δ 2.50(3H,s), 2.65(3H,s), 3.20(4H,s), 3.26(4H,s), 4.06(3H,s), 6.91(4H,m), 7.27(2H,m), 8.15(1H,s)

Example 135 ^{1}H NMR($CDCl_3$) : δ 2.18(3H,s), 2.42(3H,s), 2.57(3H,s), 3.15(4H,s), 3.30(4H,s), 4.07(3H,s), 6.84(2H,d), 7.07(3H,d), 8.13(1H,s)

Example 136 ^{1}H NMR($CDCl_3$) : δ 2.52(3H,s), 2.66(3H,s), 3.22(4H,s), 3.28(4H,s), 4.07(3H,s), 6.30(3H,m), 8.07(1H,s)

Example 137 ^{1}H NMR($CDCl_3$) : δ 2.39(3H,s), 2.58(3H,s), 2.66(3H,s), 3.04(4H,s), 3.33(4H,s), 4.07(3H,s), 7.02(1H,d), 7.10(3H,s), 8.14(1H,s)

Example 138 ^{1}H NMR($CDCl_3$) : δ 1.40(3H,d), 2.26(6H,s), 2.39(3H,s), 3.19(8H,s), 3.99(3H,s), 5.04(1H,q), 6.54(3H,s), 6.86(1H,s), 7.93(1H,s)

Example 139 ^{1}H NMR($CDCl_3$) : δ 1.40(3H,d), 2.39(3H,s), 3.20(8H,m), 3.76(6H,s), 3.99(3H,s), 5.03(1H,q), 6.03(1H,s), 6.06(2H,s), 7.04(1H,brs), 7.89(1H,s)

Example 140 ^{1}H NMR($CDCl_3$) : δ 1.40(3H,d), 2.39(3H,s), 3.19(4H,m), 3.30(4H,s), 3.97(3H,s), 5.08(1H,q), 6.89(3H,m), 7.24(2H,m), 7.87(1H,s)

Example 141 ^{1}H NMR($CDCl_3$) : δ 1.40(3H,d), 2.26(3H,s), 2.39(3H,s), 3.15(4H,s), 3.35(4H,s), 3.97(3H,s), 5.02(1H,q), 6.82(2H,d), 7.06(2H,d), 7.84(1H,s)

Example 142 ^{1}H NMR($CDCl_3$) : δ 1.40(3H,d), 2.39(3H,s), 3.20(4H,m), 3.28(4H,s), 3.98(3H,s), 5.04(1H,q), 6.27(3H,m), 7.85(1H,s)

Example 143 ^{1}H NMR($CDCl_3$) : δ 1.45(3H,d), 2.38(3H,s), 2.39(3H,s), 3.02(4H,m), 3.31(4H,s), 3.98(3H,s), 5.07(1H,q), 7.03(1H,brs), 7.09(4H,s), 7.91(1H,s)

Example 144 ^{1}H NMR($CDCl_3$) : δ 2.18(3H,s), 2.27(6H,s), 2.41(3H,s), 3.19(4H,brs), 3.22(4H,brs), 4.00(3H,s), 6.55(2H,s), 6.56(1H,s), 7.50(1H,s)

Example 145 ^{1}H NMR($CDCl_3$) : δ 2.18(3H,s), 2.41(3H,s), 3.16(4H,brs), 3.25(4H,s), 3.76(6H,s), 4.00(3H,s), 6.05(1H,s), 6.03(2H,s), 7.49(1H,s)

Example 146 ^{1}H NMR($CDCl_3$) : δ 2.18(3H,s), 2.40(3H,s), 3.18(4H,brs), 3.27(4H,brs), 4.00(3H,s), 6.27(3H,m), 7.50(1H,s)

Example 147 ^{1}H NMR($CDCl_3$) : δ 2.18(3H,s), 2.39(3H,s), 2.40(3H,s), 3.04(4H,s), 3.33(4H,s), 4.01(3H,s), 7.02(1H,d), 7.10(3H,s), 7.50(4H,s)

Example 148 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,s), 2.31(3H,s), 3.20(4H,s), 3.37(4H,s), 3.95(3H,s), 7.42(1H,s), 7.96(2H,s), 8.40(1H,s)

Example 149 ^{1}H NMR($CDCl_3$) : δ 2.09(3H,s), 2.26(3H,s), 2.31(3H,s), 3.11(4H,brs), 3.25(4H,brs), 4.00(3H,s), 6.80(2H,d), 7.06(2H,d), 7.42(1H,s)

Example 150 ^{1}H NMR($CDCl_3$) : δ 1.74(3H,d), 2.28(9H,s), 3.12(2H,brs), 3.27(4H,brs), 3.65(4H,brs), 4.02(3H,s), 4.15(1H,q), 6.54(3H,s), 8.37(1H,s)

Example 151 ^{1}H NMR($CDCl_3$) : δ 1.74(3H,d), 2.28(3H,s), 3.05(2H,brs), 3.26(4H,m), 3.67(4H,m), 3.82(6H,s), 4.01(3H,s), 4.15(1H,q), 6.06(1H,s), 6.09(2H,s), 8.37(1H,s)

Example 152 ^{1}H NMR($CDCl_3$) : δ 1.74(3H,d), 2.28(3H,s), 3.15(2H,brs),

3.22(4H,s), 3.29(4H,s), 4.00(3H,s), 4.15(1H,q), 6.30(3H,m), 8.37(1H,s)

Example 153 ^{1}H NMR($CDCl_3$) : δ 1.74(3H,d), 2.28(3H,s), 2.39(3H,s), 3.10(2H,brs), 3.04(4H,s), 3.34(4H,s), 4.07(3H,s), 4.15(1H,q), 7.02(1H,d), 7.10(3H,s), 8.37(1H,s)

Example 154 ^{1}H NMR($CDCl_3$) : δ 1.74(3H,d), 2.28(3H,s), 3.07(2H,brs), 3.20(4H,s), 3.35(4H,s), 3.90(3H,s), 4.15(1H,q), 7.97(2H,s), 8.35(1H,s), 8.42(1H,s)

Example 155 ^{1}H NMR($CDCl_3$) : δ 1.74(3H,d), 2.28(3H,s), 3.11(2H,brs), 3.20(8H,s), 4.00(3H,s), 4.15(1H,q), 6.17(1H,s), 6.74(2H,m), 8.37(1H,s)

Example 156 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 2.28(3H,s), 3.08(2H,q), 3.17(4H,s), 3.24(4H,s), 3.78(3H,s), 4.07(3H,s), 6.85(2H,d), 7.00(1H,brs), 7.07(2H,d), 8.05(1H,s)

Example 157 ^{1}H NMR($CDCl_3$) : δ 1.25(6H,m), 2.70(2H,q), 2.95(4H,t), 3.08(2H,q), 3.26(4H,brs), 3.90(3H,s), 4.07(3H,s), 7.08(2H,m), 7.18(1H,t), 7.24(1H,d), 8.40(1H,s)

Example 158 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 2.27(6H,s), 3.08(2H,q), 3.20(8H,s), 3.79(3H,s), 4.07(3H,s), 4.22(3H,s), 6.56(1H,s), 6.57(2H,s), 6.94(1H,s), 8.38(1H,s)

Example 159 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 3.07(2H,q), 3.21(8H,s), 3.77(6H,s), 3.79(3H,s), 4.07(3H,s), 6.05(1H,s), 6.09(2H,s), 6.95(1H,s), 8.37(1H,s)

Example 160 ^{1}H NMR($CDCl_3$) : δ 1.27(3H,t), 3.07(2H,q), 3.24(8H,s), 3.81(3H,s), 4.08(3H,s), 6.75(2H,s), 6.83(1H,s), 7.05(1H,brs), 8.29(1H,s)

Example 161 ^{1}H NMR($CDCl_3$) : δ 1.27(3H,t), 2.40(3H,s), 3.07(6H,m), 3.28(4H,brs), 3.88(3H,s), 4.07(3H,s), 7.05(2H,m), 7.12(3H,m), 8.38(1H,s)

Example 162 ^{1}H NMR($CDCl_3$) : δ 1.27(3H,t), 1.40(6H,t), 3.07(2H,q), 3.26(4H,s), 3.34(4H,s), 3.77(3H,s), 4.08(3H,s), 4.39(4H,q), 7.00(1H,brs), 7.70(2H,s), 8.17(1H,s), 8.35(1H,s)

Example 163 ^{1}H NMR($CDCl_3$) : δ 1.27(3H,t), 3.07(2H,q), 3.22(8H,d), 3.80(3H,s), 4.08(3H,s), 6.29(1H,t), 6.36(2H,d), 6.99(1H,brs), 8.32(1H,s)

Example 164 ^{1}H NMR($CDCl_3$) : δ 1.25(3H,t), 2.27(3H,s), 2.69(2H,q),

3.14(4H,d), 3.22(4H,d), 4.01(3H,s), 4.60(2H,s), 6.82(2H,d), 6.96(1H,brs), 7.06(2H,d), 7.78(1H,s)

Example 165 ^{1}H NMR($CDCl_3$) : δ 1.21(3H,t), 1.26(3H,t), 2.67(4H,m), 2.91(4H,t), 3.27(4H,s), 4.01(3H,s), 4.66(2H,s), 7.06(2H,m), 7.16(1H,t), 7.21(1H,d), 7.82(1H,s)

Example 166 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 2.27(6H,s), 2.69(2H,q), 3.19(8H,d), 4.02(3H,s), 4.60(2H,s), 6.55(3H,s), 6.90(1H,s), 7.80(1H,s)

Example 167 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 2.69(2H,q), 3.19(8H,s), 3.76(6H,s), 4.02(3H,s), 4.60(2H,s), 6.03(1H,s), 6.08(2H,d), 6.88(1H,s), 7.79(1H,s)

Example 168 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 2.69(2H,q), 3.20(8H,s), 4.01(3H,s), 4.62(2H,s), 6.73(2H,s), 6.84(1H,s), 6.95(1H,brs), 7.77(1H,s)

Example 169 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 2.39(3H,s), 2.70(2H,q), 3.03(4H,d), 3.28(4H,s), 4.01(3H,s), 4.65(2H,s), 7.03(2H,m), 7.10(3H,m), 7.80(1H,s)

Example 170 ^{1}H NMR($CDCl_3$) : δ 1.20(3H,t), 2.61(2H,q), 3.09(4H,s), 3.23(4H,s), 3.97(3H,s), 4.45(4H,s), 4.46(2H,s), 6.77(1H,s), 6.81(2H,s), 6.99(1H,brs), 7.90(1H,s)

Example 171 ^{1}H NMR($CDCl_3$) : δ 1.25(3H,t), 2.68(2H,q), 3.21(4H,s), 3.22(4H,s), 4.01(3H,s), 4.62(2H,s), 6.27(1H,t), 6.33(2H,d), 7.05(1H,brs), 7.76(1H,s)

Example 172 ^{1}H NMR($CDCl_3$) : δ 3.24(8H,s), 3.76(6H,s), 4.15(3H,s), 6.00(1H,s), 6.08(2H,d), 7.31(1H,t), 7.35(1H,s), 7.43(1H,t), 7.57(1H,d), 7.71(1H,d), 8.06(1H,s)

Example 173 ^{1}H NMR($CDCl_3$) : δ 2.28(6H,s), 3.25(4H,s), 3.26(4H,s), 4.18(3H,s), 6.33(1H,brs), 6.56(1H,s), 6.58(2H,d), 7.33(1H,t), 7.47(1H,t), 7.57(1H,d), 7.78(1H,d), 8.05(1H,s)

Example 174 ^{1}H NMR($CDCl_3$) : δ 3.26(8H,s), 4.18(3H,s), 6.29(1H,t), 6.36(2H,d), 7.25(1H,brs), 7.34(1H,t), 7.49(1H,t), 7.50(1H,d), 7.79(1H,d), 8.02(1H,s)

Example 175 ^{1}H NMR($CDCl_3$) : δ 3.16(4H,s), 3.36(4H,s), 3.84(3H,s),

4.18(3H,s), 6.86(1H,d), 6.95(2H,m), 7.02(1H,m), 7.34(1H,t), 7.48(1H,t), 7.60(1H,d), 7.78(1H,d), 8.04(1H,s)

Example 176 ^{1}H NMR($CDCl_3$) : δ 3.25(4H,d), 3.32(4H,s), 4.18(3H,s), 6.77(1H,d), 6.85(2H,m), 7.17(1H,t), 7.35(1H,t), 7.50(1H,t), 7.59(1H,d), 7.79(1H,d), 7.99(1H,s)

Example 177 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.20(3H,s), 3.18(4H,d), 3.23(4H,d), 3.84(3H,s), 6.65(1H,s), 6.87(1H,t), 6.91(2H,d), 6.93(1H,brs), 7.25(2H,m), 7.36(1H,s)

Example 178 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.20(3H,s), 2.27(3H,s), 3.12(4H,d), 3.22(4H,d), 3.84(3H,s), 6.64(1H,s), 6.83(2H,d), 6.96(1H,brs), 7.07(2H,d), 7.35(1H,s)

Example 179 ^{1}H NMR($CDCl_3$) : δ 1.21(3H,t), 2.20(3H,s), 2.21(3H,s), 2.67(2H,q), 2.90(4H,t), 3.26(4H,s), 3.85(3H,s), 6.65(1H,s), 7.07(3H,m), 7.17(1H,t), 7.21(1H,d), 7.36(1H,s)

Example 180 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.20(3H,s), 2.27(6H,s), 3.16(4H,d), 3.20(4H,d), 3.85(3H,s), 6.54(1H,s), 6.56(2H,s), 6.64(1H,s), 6.89(1H,brs), 7.37(1H,s)

Example 181 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.20(3H,s), 3.17(4H,s), 3.19(4H,s), 3.77(6H,s), 3.85(3H,s), 6.03(1H,s), 6.08(2H,d), 6.64(1H,s), 6.90(1H,brs), 7.36(1H,s)

Example 182 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.20(3H,s), 3.22(8H,s), 3.85(3H,s), 6.28(1H,t), 6.36(2H,d), 6.64(1H,s), 6.89(1H,brs), 7.36(1H,s)

Example 183 ^{1}H NMR($CDCl_3$) : δ 2.15(3H,s), 2.20(3H,s), 3.17(4H,d), 3.21(4H,d), 3.85(3H,s), 6.65(1H,s), 6.78(1H,d), 6.81(1H,d), 6.86(1H,s), 6.94(1H,brs), 7.16(1H,t), 7.33(1H,s)

Example 184 ^{1}H NMR($CDCl_3$) : δ 2.15(3H,s), 2.20(3H,s), 3.17(4H,d), 3.21(4H,d), 3.85(3H,s), 6.65(1H,s), 6.81(1H,d), 6.96(2H,brd), 7.02(1H,s), 7.10(1H,t), 7.33(1H,s)

Example 185 ^{1}H NMR($CDCl_3$) : δ 2.19(3H,s), 2.21(3H,s), 2.39(3H,s), 3.00(4H,d), 3.28(4H,s), 3.85(3H,s), 6.64(1H,s), 6.99(1H,brs), 7.03(1H,d), 7.10(3H,m), 7.36(1H,s)

Example 186 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.33(3H,s), 3.19(4H,s), 3.20(4H,s), 3.78(3H,s), 3.98(3H,s), 6.84(1H,s), 6.87(1H,t), 6.93(2H,m), 7.24(1H,d), 7.56(1H,s)

Example 187 ^{1}H NMR($CDCl_3$) : δ 2.13(3H,s), 2.27(3H,s), 2.32(3H,s), 3.13(4H,d), 3.19(4H,d), 3.77(3H,s), 3.98(3H,s), 6.81(1H,s), 6.83(2H,d), 7.07(2H,d), 7.54(1H,s)

Example 188 ^{1}H NMR($CDCl_3$) : δ 2.13(3H,s), 2.28(9H,s), 3.17(4H,brs), 3.78(3H,s), 3.98(3H,s), 6.56(3H,s), 6.70(1H,s), 7.53(1H,s)

Example 189 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.32(3H,s), 3.17(8H,s), 3.77(9H,s), 3.98(3H,s), 6.04(1H,s), 6.08(2H,s), 6.81(1H,s), 7.53(1H,s)

Example 190 ^{1}H NMR($CDCl_3$) : δ 2.15(3H,s), 2.33(3H,s), 3.17(8H,s), 3.78(3H,s), 3.98(3H,s), 6.28(1H,t), 6.35(2H,d), 6.78(1H,s), 7.50(1H,s)

Example 191 ^{1}H NMR($CDCl_3$) : δ 2.15(3H,s), 2.34(3H,s), 2.38(3H,s), 3.00(4H,s), 3.28(4H,s), 3.78(3H,s), 3.90(3H,s), 7.01(1H,s), 7.10(3H,s), 7.55(1H,s)

Example 192 ^{1}H NMR($CDCl_3$) : δ 2.16(3H,s), 2.34(3H,s), 3.20(4H,s), 3.37(4H,s), 3.78(3H,s), 3.90(3H,s), 6.78(1H,s), 7.47(1H,s), 7.97(2H,s), 8.42(1H,s)

Example 193 ^{1}H NMR($CDCl_3$) : δ 1.15(3H,t), 2.37(3H,s), 2.50(2H,q), 3.18(4H,brs), 3.23(4H,brs), 3.82(3H,s), 3.97(3H,s), 6.72(2H,s), 6.88(1H,s), 7.45(1H,s)

Example 194 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 3.07(2H,q), 3.22(8H,s), 3.79(3H,s), 3.86(3H,s), 4.07(3H,s), 6.29(1H,t), 6.36(2H,d), 8.29(1H,s)

Example 195 ^{1}H NMR($CDCl_3$) : δ 1.26(3H,t), 1.40(6H,t), 3.06(2H,q), 3.27(4H,brs), 3.38(4H,brs), 3.77(3H,s), 3.81(3H,s), 4.07(3H,s), 4.38(4H,q), 7.76(2H,s), 8.17(1H,s), 8.30(1H,s)

Example 196 ^{1}H NMR($CDCl_3$) : δ 1.24(3H,t), 2.67(2H,q), 3.21(8H,s), 3.78(3H,s), 4.01(3H,s), 4.59(2H,s), 4.63(4H,s), 6.84(2H,m), 6.88(2H,s), 7.78(1H,s)

Example 197 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.20(3H,s), 2.27(3H,s), 3.13(4H,brs), 3.24(4H,brs), 3.78(3H,s), 3.84(3H,s), 6.64(1H,s), 6.84(2H,brs),

7.07(2H,d), 7.27(1H,brs)

Example 198 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,s), 2.20(3H,s), 2.25(6H,s), 3.16(4H,brs), 3.22(4H,brs), 3.79(3H,s), 3.83(3H,s), 6.54(2H,s), 6.64(1H,s), 6.81(1H,brs), 7.27(1H,brs)

Example 199 ^{1}H NMR($CDCl_3$) : δ 2.11(3H,brs), 2.16(3H,s), 2.36(3H,s), 3.24(4H,t), 3.80(4H,s), 3.92(3H,s), 6.85(1H,brs), 6.89(1H,t), 6.95(2H,d), 7.28(2H,t)

Example 200 ^{1}H NMR($CDCl_3$) : δ 2.11(3H,brs), 2.16(3H,s), 2.28(3H,s), 2.36(3H,s), 3.19(4H,t), 3.80(4H,brs), 3.92(3H,s), 6.86(3H,brd), 7.08(2H,d)

Example 201 ^{1}H NMR($CDCl_3$) : δ 0.92(3H,t), 1.35(2H,m), 1.55(2H,m), 2.10(3H,brs), 2.16(3H,s), 2.36(3H,s), 2.54(2H,t), 3.20(4H,t), 3.80(4H,brs), 3.92(3H,s), 6.87(3H,brd), 7.09(2H,d)

Example 202 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,brs), 2.16(3H,s), 2.89(6H,s), 2.36(3H,s), 3.21(4H,t), 3.78(4H,brs), 3.92(3H,s), 6.56(1H,s), 6.59(2H,s), 6.84(3H,brs)

Example 203 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,brs), 2.16(3H,s), 2.36(3H,s), 3.22(4H,t), 3.79(7H,brs), 3.92(3H,s), 6.84(1H,brs), 6.95(4H,s)

Example 204 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,brs), 2.16(3H,s), 2.36(3H,s), 3.24(4H,brs), 3.78(10H,s), 3.92(3H,s), 6.05(1H,s), 6.11(2H,s), 6.84(3H,brs)

Example 205 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,brs), 2.16(3H,s), 2.36(3H,s), 3.24(4H,t), 3.78(4H,t), 6.28(1H,t), 6.39(2H,d), 6.84(1H,s)

Example 206 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,s), 2.16(3H,s), 2.36(3H,s), 3.25(4H,t), 3.78(4H,t), 3.92(3H,s), 6.77(2H,s), 6.84(2H,s)

Example 207 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,brs), 2.17(3H,s), 2.36(3H,s), 3.25(4H,brs), 3.79(4H,brs), 3.92(3H,s), 6.84(2H,m), 7.00(1H,d), 7.06(1H,brs), 7.13(1H,t)

Example 208 ^{1}H NMR($CDCl_3$) : δ 2.12(3H,s), 2.17(3H,s), 2.37(3H,s), 3.50(4H,t), 3.88(4H,brs), 3.93(3H,s), 6.87(1H,brs), 8.00(2H,d), 8.43(1H,s)

Example 209 ^{1}H NMR($CDCl_3$) : δ 1.41(6H,t), 2.11(3H,brs), 2.15(3H,s), 2.37(3H,s), 3.36(4H,brs), 3.83(4H,brs), 3.92(3H,s), 4.40(4H,q), 6.85(1H,brs), 7.78(2H,s), 8.18(1H,s)

Example 210 ^{1}H NMR($CDCl_3$) : δ 1.67(3H,t), 2.10(3H,s), 2.39(3H,s), 2.51(2H,q), 3.25(4H,t), 3.80(4H,t), 3.92(3H,s), 6.90(2H,t), 6.95(2H,d), 7.29(2H,t)

Example 211 ^{1}H NMR($CDCl_3$) : δ 1.17(3H,t), 2.10(3H,brs), 2.39(3H,s), 2.52(2H,q), 3.13(4H,brs), 3.84(4H,brs), 3.88(3H,s), 3.93(3H,s), 6.89(2H,brd), 6.93(2H,m), 7.04(1H,m)

Example 212 ^{1}H NMR($CDCl_3$) : δ 1.16(3H,t), 2.09(3H,s), 2.39(3H,s), 2.51(2H,q), 3.23(4H,t), 3.79(10H,s), 3.92(3H,s), 6.05(1H,s), 6.11(2H,d), 6.87(1H,s)

Example 213 ^{1}H NMR($CDCl_3$) : δ 1.18(3H,t), 1.25(3H,t), 2.11(3H,brs), 2.40(3H,s), 2.52(2H,q), 2.72(2H,q), 2.96(4H,brs), 3.79(4H,brs), 3.94(3H,s), 6.88(1H,brs), 7.09(2H,m), 7.18(1H,t), 7.24(1H,d)

Example 214 ^{1}H NMR($CDCl_3$) : δ 1.16(3H,t), 2.09(3H,s), 2.29(6H,s), 2.39(3H,s), 2.51(2H,q), 3.22(4H,t), 3.78(4H,t), 3.92(3H,s), 6.56(1H,s), 6.59(2H,s), 6.87(1H,s)

Example 215 ^{1}H NMR($CDCl_3$) : δ 1.16(3H,t), 2.11(3H,brs), 2.40(3H,s), 2.51(2H,q), 3.27(4H,s), 3.80(4H,s), 3.92(3H,s), 6.28(1H,t), 6.39(2H,d), 6.84(1H,s)

Example 216 ^{1}H NMR($CDCl_3$) : δ 1.17(3H,t), 2.12(3H,brs), 2.40(3H,s), 2.52(2H,q), 3.27(4H,s), 3.80(4H,s), 3.92(3H,s), 6.77(2H,d), 6.84(1H,s), 6.90(1H,brs)

Example 217 ^{1}H NMR($CDCl_3$) : δ 1.15(3H,t), 2.03(3H,brs), 2.38(3H,s), 2.50(2H,q), 2.90(4H,brs), 3.51(4H,brs), 3.90(3H,s), 6.82(1H,d), 7.03(1H,d), 7.10(1H,t), 7.27(3H,m), 7.39(2H,t), 7.61(2H,d)

Example 218 ^{1}H NMR($CDCl_3$) : δ 1.15(3H,t), 2.13(3H,brs), 2.41(3H,s), 2.52(2H,q), 3.52(4H,brs), 3.93(7H,s), 6.87(1H,brs), 7.99(2H,d), 8.44(1H,s)

Example 219 ^{1}H NMR($CDCl_3$) : δ 1.17(3H,t), 2.10(3H,brs), 2.39(3H,s), 2.42(3H,s), 2.52(2H,q), 3.06(4H,s), 3.83(4H,s), 3.93(3H,s), 6.88(1H,brs), 7.05(1H,m), 7.12(3H,s)

Example 220 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,brs), 2.73(3H,s), 3.23(4H,brs), 3.86(10H,s), 3.89(3H,s), 6.05(1H,s), 6.11(2H,s), 7.62(1H,brs)

Example 221 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,brs), 2.29(6H,s), 2.73(3H,s), 3.23(4H,brs), 3.82(4H,brs), 3.86(3H,s), 3.99(3H,s), 6.57(3H,m), 7.62(1H,brs)

Example 222 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,s), 2.73(3H,s), 3.27(4H,t), 3.83(4H,s), 3.86(3H,s), 4.00(3H,s), 6.30(1H,t), 6.40(2H,d), 7.64(1H,brs)

Example 223 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,brs), 2.73(3H,s), 3.14(4H,brs), 3.86(7H,s), 3.89(3H,s), 4.00(3H,s), 6.89(1H,d), 6.95(2H,m), 7.04(1H,brm), 7.62(1H,brs)

Example 224 ^{1}H NMR($CDCl_3$) : δ 2.11(3H,brs), 2.73(3H,s), 3.26(4H,t), 3.85(7H,s), 4.00(3H,s), 6.91(1H,t), 6.95(2H,d), 7.30(2H,t), 7.63(1H,brs)

Example 225 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,s), 2.27(3H,s), 2.72(3H,s), 3.20(4H,t), 3.83(4H,s), 3.85(3H,s), 4.00(3H,s), 6.87(2H,d), 7.09(3H,d), 7.63(1H,brs)

Example 226 ^{1}H NMR($CDCl_3$) : δ 2.11(3H,brs), 2.73(3H,s), 3.27(4H,brs), 3.86(7H,s), 4.00(3H,s), 6.81(1H,d), 6.85(1H,d), 6.90(1H,s), 7.19(1H,t), 7.63(1H,brs)

Example 227 ^{1}H NMR($CDCl_3$) : δ 2.12(3H,brs), 2.29(6H,s), 2.53(3H,s), 2.67(3H,s), 3.24(4H,brs), 3.83(4H,brs), 4.00(3H,s), 6.58(1H,s), 6.60(2H,s), 7.47(1H,brs)

Example 228 ^{1}H NMR($CDCl_3$) : δ 2.12(3H,brs), 2.53(3H,s), 2.68(3H,s), 3.25(4H,t), 3.79(6H,s), 3.82(4H,brs), 4.00(3H,s), 6.06(1H,s), 6.12(2H,d), 7.46(1H,brs)

Example 229 ^{1}H NMR($CDCl_3$) : δ 2.12(3H,s), 2.53(3H,s), 2.68(3H,s), 3.26(4H,t), 3.77(4H,t), 4.00(3H,s), 6.89(3H,d), 7.19(2H,d), 7.46(1H,s)

Example 230 ^{1}H NMR($CDCl_3$) : δ 2.12(3H,brs), 2.12(3H,s), 2.53(3H,s), 2.68(3H,s), 3.22(4H,s), 3.85(3H,brs), 4.00(3H,s), 6.87(2H,d), 7.10(2H,d), 7.45(1H,s)

Example 231 ^{1}H NMR($CDCl_3$) : δ 2.12(3H,s), 2.55(3H,s), 2.68(3H,s), 3.32(4H,brs), 3.86(4H,brs), 4.01(3H,s), 6.38(3H,m), 7.47(1H,brs)

Example 232 ^{1}H NMR($CDCl_3$) : δ 2.12(3H,s), 2.43(3H,s), 2.54(3H,s), 2.68(3H,s), 3.07(4H,brs), 3.86(4H,brs), 4.00(3H,s), 7.06(1H,m), 7.13(3H,m), 7.46(1H,brs)

Example 233 ^{1}H NMR($CDCl_3$) : δ 1.28(3H,t), 2.13(3H,brs), 2.29(3H,s), 3.11(2H,q), 3.21(4H,brs), 3.85(7H,brs), 4.00(3H,s), 6.89(2H,brs), 7.08(2H,d), 7.62(1H,brs)

Example 234 ^{1}H NMR($CDCl_3$) : δ 1.24(3H,t), 1.28(3H,t), 2.12(3H,brs), 2.72(2H,q), 2.96(4H,brs), 3.10(2H,q), 3.81(4H,brs), 3.86(3H,s), 4.00(3H,s), 7.09(2H,m), 7.19(1H,t), 7.24(1H,d), 7.60(1H,brs)

Example 235 ^{1}H NMR($CDCl_3$) : δ 1.28(3H,t), 2.10(3H,brs), 2.29(6H,s), 3.11(2H,q), 3.23(4H,brs), 3.82(4H,brs), 3.85(3H,s), 4.00(3H,s), 6.57(1H,s), 6.59(2H,s), 7.59(1H,brs)

Example 236 ^{1}H NMR($CDCl_3$) : δ 1.28(3H,t), 2.10(3H,brs), 3.10(2H,q), 3.24(4H,brs), 3.79(6H,s), 3.81(4H,brs), 3.85(3H,s), 4.00(3H,s), 6.06(1H,s), 6.11(2H,s), 7.59(1H,brs)

Example 237 ^{1}H NMR($CDCl_3$) : δ 1.28(3H,t), 2.10(3H,brs), 3.11(2H,q), 3.28(4H,brs), 3.82(4H,brs), 3.85(3H,s), 4.00(3H,s), 6.77(2H,d), 6.85(1H,s), 7.60(1H,brs)

Example 238 ^{1}H NMR($CDCl_3$) : δ 1.28(3H,t), 2.10(3H,brs), 2.43(3H,s), 3.06(6H,m), 3.86(7H,brs), 4.01(3H,s), 7.06(1H,s), 7.12(3H,s), 7.60(1H,brs)

Example 239 ^{1}H NMR($CDCl_3$) : δ 1.28(3H,t), 1.43(6H,t), 2.11(3H,brs), 3.12(2H,q), 3.37(4H,brs), 3.86(7H,s), 4.01(3H,s), 4.41(4H,q), 7.60(1H,brs), 7.79(2H,s), 8.18(1H,s)

Example 240 ^{1}H NMR($CDCl_3$) : δ 1.28(3H,t), 2.10(3H,brs), 3.10(2H,q), 3.28(4H,brs), 3.82(4H,brs), 3.86(3H,s), 4.00(3H,s), 6.30(1H,t), 6.39(2H,d), 7.60(1H,brs)

Example 241 ^{1}H NMR($CDCl_3$) : δ 2.07(3H,s), 3.27(4H,t), 3.79(6H,s), 3.86(4H,t), 4.10(3H,s), 6.06(1H,m), 6.12(2H,d), 7.32(1H,t), 7.36(1H,s), 7.48(1H,t), 7.61(1H,d), 7.80(1H,d)

Example 242 ^{1}H NMR($CDCl_3$) : δ 2.07(3H,s), 2.30(6H,s), 3.25(4H,s), 3.86(4H,s), 4.10(3H,s), 6.58(1H,s), 6.60(2H,s), 7.32(1H,t), 7.36(1H,s), 7.49(1H,d), 7.80(1H,d)

Example 243 ^{1}H NMR($CDCl_3$) : δ 2.09(3H,brs), 3.27(4H,s), 3.87(4H,s), 4.10(3H,s), 6.29(1H,t), 6.39(2H,d), 7.32(1H,t), 7.37(1H,s), 7.49(1H,t),

7.80(1H,d)

Example 244 ^{1}H NMR($CDCl_3$) : δ 2.09(3H,brs), 3.15(4H,t), 3.89(4H,s), 4.11(3H,s), 6.89(1H,d), 6.96(2H,m), 7.04(1H,m), 7.32(1H,t), 7.38(1H,brs), 7.48(1H,t), 7.62(1H,d), 7.80(1H,d)

Example 245 ^{1}H NMR($CDCl_3$) : δ 2.10(3H,brs), 3.29(4H,t), 3.88(4H,brs), 4.10(3H,s), 6.82(1H,dd), 6.88(1H,d), 6.92(1H,s), 7.20(1H,t), 7.33(1H,t), 7.40(1H,brs), 7.49(1H,t), 7.62(1H,d), 7.80(1H,d)

Example 246 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,brs), 2.17(3H,s), 2.22(3H,s), 3.25(4H,t), 3.78(7H,s), 6.60(1H,brs), 6.66(1H,s), 6.89(1H,t), 6.95(2H,t), 7.29(2H,t)

Example 247 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,brs), 2.17(3H,s), 2.22(3H,s), 2.28(3H,s), 3.19(4H,t), 3.77(7H,s), 6.60(1H,brs), 6.66(1H,s), 6.86(2H,d), 7.08(2H,d)

Example 248 ^{1}H NMR($CDCl_3$) : δ 1.25(3H,t), 2.14(3H,brs), 2.18(3H,s), 2.23(3H,s), 2.72(2H,q), 2.96(4H,brs), 3.75(4H,brs), 3.79(3H,s), 6.60(1H,brs), 6.67(1H,s), 7.08(2H,t), 7.18(1H,t), 7.24(1H,m)

Example 249 ^{1}H NMR($CDCl_3$) : δ 2.12(3H,s), 2.16(3H,s), 2.22(3H,s), 2.29(6H,s), 3.21(4H,t), 3.74(4H,t), 3.77(3H,s), 6.55(1H,s), 6.59(3H,s), 6.65(1H,s)

Example 250 ^{1}H NMR($CDCl_3$) : δ 2.12(3H,s), 2.16(3H,s), 2.22(3H,s), 3.23(4H,t), 3.74(4H,t), 3.77(3H,s), 3.78(6H,s), 6.04(1H,s), 6.12(2H,d), 6.59(1H,s), 6.65(1H,s)

Example 251 ^{1}H NMR($CDCl_3$) : δ 2.11(3H,s), 2.16(3H,s), 2.22(3H,s), 3.25(4H,t), 3.74(4H,t), 3.77(3H,s), 6.28(1H,t), 6.39(2H,d), 6.59(1H,s), 6.66(1H,s)

Example 252 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,brs), 2.17(3H,s), 2.22(3H,s), 3.25(4H,t), 3.76(4H,brs), 3.78(3H,s), 6.61(1H,brs), 6.66(1H,s), 6.83(2H,m), 6.90(1H,s), 7.18(1H,t)

Example 253 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,brs), 2.17(3H,s), 2.23(3H,s), 3.25(4H,t), 3.78(7H,s), 6.61(1H,brs), 6.66(1H,s), 6.85(1H,d), 6.98(1H,d), 7.06(1H,s), 7.12(1H,t)

Example 254 ^{1}H NMR($CDCl_3$) : δ 2.14(3H,brs), 2.17(3H,s), 2.22(3H,s), 2.42(3H,s), 3.06(4H,t), 3.78(7H,s), 6.60(1H,brs), 6.66(1H,s), 7.06(1H,m), 7.12(3H,s)

Antitumor activities of the compounds of the present invention were tested *in vitro* against 5 kinds of human tumor cell lines and a leukemia tumor cell line. The method and result of the *in vitro* tests is as follows.

Experimental 1 : In vitro antitumor effect against human tumor cell lines.

A. Tumor cell line : A549 (human non-small lung cell)
SKOV-3 (human ovarian)
HCT-15 (human colon)
XF 498 (human CNS)
SKMEL-2 (human melanoma)

B. SRB Assay Method.

a. Human solid tumor cell lines, A549(non-small lung cell), SKMEL-2(melanoma), HCT-15(colon), SKOV-3(ovarian), XF-498(CNS) were cultured at 37℃ in 5% CO_2 incubators using RPMI 1640 media containing 10% FBS, while they were transfer-cultured successively once or twice per week. Cell cultures were dissolved in a solution of 0.25% trypsin and 3 mM CDTA PBS(-) and then cells were separated from media which the cells were sticked on.

b. $5\times10^3\sim2\times10^4$ cells were added into each well of 96-well plate and cultured in 5% CO_2 incubator, at 37℃, for 24 hours.

c. Each sample drug was dissolved in a little DMSO and diluted with the used medium to a prescribed concentration for experiments, wherein the final concentration of DMSO was controlled below 0.5%.

d. Medium of each well cultured for 24 hours as above b. was removed by aspiration. Each 200 μl of drug samples prepared in c. was added into each well and the wells were cultured for 48 hours. Tz(time zero) plates were collected at the point of time drugs were added.

e. According to the SRB assay method, cell fixing with TCA, staining with 0.4% SRB solution, washing with 1% acetic acid and elution of dye with 10mM Tris solution were carried out on Tz plates and culture-ended plates, whereby OD values were measured at 520 nm.

C. Calculation of result

a. Time zero(Tz) value was determined with measuring the SRB protein amounts of the Tz plates collected at the point of time drugs were added.

b. Control value(C) was determined with the OD values of wells untreated with a drug.

c. Drug-treated test value(T) was determined with the OD values of drug-treated wells.

d. Effects of drugs were estimated with growth stimulation, net growth inhibition, net killing etc., being calculated from Tz, C and T.

e. If $T \geq Tz$, cellular response function was calculated by $100x(T-Tz)/(C-Tz)$, and if $T < Tz$, by $100\times(T-Tz)/Tz$. The results are shown in the next table 1.

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D. Results.

It was found that all the tested compounds of the present invention have superior antitumor activities to the control, cisplatin.

Table 1.

ED_{50}=㎍/㎖

Example No.	A 549	SK-OV-3	SK-MEL-2	XF-498	HCT 15
2	0.032	0.088	0.029	0.084	0.019
3	0.0016	0.0064	0.0015	0.0022	0.0020
4	0.047	0.251	0.042	0.089	0.038
7	0.0024	0.0072	0.0023	0.0027	0.0028
12	0.008	0.069	0.008	0.017	0.001
14	0.204	0.677	0.283	0.340	0.067
15	0.079	0.184	0.038	0.096	0.071
19	0.0064	0.143	0.043	0.093	0.080
20	0.323	0.904	0.211	0.970	0.295
21	0.038	0.093	0.024	0.097	0.008
28	0.0001	0.0006	<0.0001	0.0001	0.0001
30	0.0006	0.0007	<0.0001	0.0005	0.0007
34	0.0023	0.0038	0.0003	0.0021	0.0021
35	0.0001	0.0007	<0.0001	0.0001	0.0001
37	0.01	0.02	0.02	0.003	0.009
38	0.00003	0.00009	0.00004	0.00011	0.00013
39	0.10	0.33	0.07	0.14	0.06
40	0.41	1.01	0.37	0.81	0.39
42	0.0018	0.0043	0.0012	0.0057	0.0026

Example No.	A 549	SK-OV-3	SK-MEL-2	XF-498	HCT 15
45	0.0001	0.0002	<0.0001	0.0002	0.0001
46	0.002	0.007	0.003	0.001	0.002
48	0.001	0.007	0.0003	0.004	0.002
51	0.37	0.68	0.28	0.63	0.18
53	0.17	0.21	0.93	0.27	0.05
55	0.34	0.49	0.22	0.41	0.33
64	0.019	0.057	0.011	0.014	0.032
66	0.005	0.008	0.002	0.008	0.003
68	0.38	0.86	0.34	0.47	0.31
72	0.0001	0.0007	<0.0001	0.0001	0.0001
74	0.0020	0.038	0.003	0.024	0.028
86	0.04	0.08	0.03	0.04	0.06
87	0.01	0.03	0.66	0.08	0.008
89	0.04	0.20	0.03	0.04	0.05
90	0.38	0.35	0.90	0.68	0.20
99	0.012	0.008	0.006	0.010	0.003
101	0.0003	0.0003	0.0003	0.0002	0.0001
107	0.032	0.013	0.005	0.008	0.009
118	0.057	0.032	0.019	0.017	0.0002
120	0.64	0.73	0.28	0.82	0.30
125	0.0009	0.0008	0.0001	0.0001	0.0001
127	0.013	0.011	0.005	0.006	0.002
132	0.011	0.007	0.001	0.002	0.001
133	0.0001	0.0001	0.0001	0.0001	0.0001
138	0.074	0.030	0.016	0.018	0.006
139	0.0007	0.0007	0.0002	0.0003	0.0004

Example No.	A 549	SK-OV-3	SK-MEL-2	XF-498	HCT 15
159	0.029	0.010	0.002	0.006	0.0006
172	0.07	0.08	0.02	0.03	0.02
173	0.40	0.86	0.15	0.21	0.18
176	0.0012	0.0009	0.0003	0.0001	0.0001
177	0.0006	0.0008	0.0003	0.0004	0.0001
180	0.28	0.16	0.31	0.24	0.16
181	0.13	0.06	0.11	0.04	0.02
182	0.292	0.081	0.033	0.103	0.006
Cisplatin	0.91	1.32	0.87	0.77	3.17

Experimental 2.

In vitro antitumor effects against animal leukemia cells.

A. Material :

Tumor cell line : P388 (mouse lymphoid neoplasma cell)

B. Method : Dye Exclusion Assay.

1) Concentrations of P388 cells being cultured in RPMI 1640 media containing 10% FBS were regulated to 1×10^6 cells/ml.

2) Sample drugs of respective concentrations diluted in the ratio of log doses were added into each cell culture and cultured at 37℃, for 48 hours, in 50% CO_2 incubator, and then viable cell numbers were measured by dye exclusion test using trypan blue.

3) Concentrations of sample compounds showing 50 % cell growth inhibition compared with the control(IC_{50}) were determined and listed in the table 2 below.

* REFERENCE

1) P. Skehan, R. Strong, D. Scudiero, A. Monks, J. B. Mcmahan, D. T. Vistica, J. Warren, H. Bokesh, S. Kenney and M. R. Boyd. : Proc. Am.

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2) L. V. Rubinstein, R. H. Shoemaker, K. D. Paull, R. M. Simon, S. Tosini, P. Skehan, D. Scudiero, A. Monks, J. Natl. Cancer Inst., 82, 1113(1990)

3) P. Skehan, R. Strong, D. Scudiero, J. B. Mcmahan, D. T. Vistica, J. Warren, H. Bokesch, S. Kenney and M. R. Boyd. : J. Natl. Cancer Inst., 82, 1107(1990)

C. Results

As the results of measurement of antitumor activities of compounds of the present invention against P388 mouse leukemia cells, it was found that all the compounds tested have equal to or higher antitumor activities than those of the control drug, mitomycin C.

Example No.	P388	Example No.	P388
2	0.3	46	0.2
3	0.01	48	0.39
7	0.02	64	0.34
11	0.02	66	0.2
12	0.1	72	0.10
15	0.70	74	0.68
19	0.2	99	0.04
20	1.2	101	0.002
21	0.8	107	0.04
28	0.04	118	0.3
30	0.07	138	0.1
34	0.14	139	0.03
35	0.01	173	0.4
37	0.3	180	0.05
38	0.01	181	0.03
42	0.03	182	0.2
45	0.15	Mitomycin C	1.1

Experimental 3.

Acute toxicity test (LD_{50}) :

A. Method : Litchfield-Wilcoxon method.

6 weeks old ICR mice(male 30±2.0g) were fed freely with solid feed and water at room temperature, 23±1℃ at humidity 60±5%. Sample drugs were injected into abdominal cavities of mice, while each group comprises 6 mice. Observed during 14 days, external appearances and life or death were recorded, and then, visible pathogenies were observed from dead animals by dissection. LD_{50} value was calculated by

Litchfiled-wilcoxon method.

B. Result

The results are shown at the next table 3.

Table 3

Example No.	LD_{50}(mg/kg)		
	p.o.	i.v.	i.p.
7		75	
38	410	97	
99		>200	
104		212	
Cisplatin			9.7

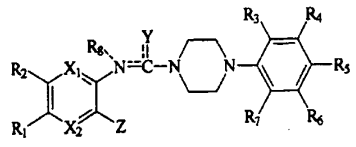
As described above, it was found that the compounds of the present invention are more safer than cisplatin, whereby the present compounds may solve problems of known drugs by the prior art such as restriction of dosage, toxicity, etc.

[redacted]

Claims

What is claimed:

1. A compound of the general formula(I)



(I)

wherein R_1 and R_2 are independently hydrogen, C_1-C_4 alkyl, C_1-C_4 alkylcarboxyl, C_1-C_4 alkylcarbonyl, C_1-C_4 alkoxy, C_1-C_4 hydroxyalkyl, C_1-C_4 aminoalkyl or C_1-C_4 hydroxyiminoalkyl, or R_1 and R_2 are fused to form C_3-C_4 unsaturated ring;

R_3, R_4, R_5, R_6 and R_7 are independently hydrogen, halogen, hydroxy, nitro, amino, C_1-C_4 alkyl, C_1-C_4 alkylcarboxyl, C_1-C_4 alkylcarbonyl, C_1-C_4 alkoxy or C_1-C_4 thioalkoxy;

R_8 is C_1-C_4 alkyl;

Y is oxygen, sulphur, amino, substituted amino or C_1-C_4 thioalkyl;

Z is C_1-C_4 alkoxy, C_1-C_4 alkyl, C_1-C_4 alkylamino or C_1-C_4 thioalkoxy;

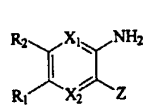
X_1 and X_2 are independently carbon or nitrogen; and

—N=C— and —C=Y— may form a single bond or a double bond provided that if —N=C— forms a single bond, —C=Y— forms a bouble bond, and if —C=Y— forms a single bond, —N=C— forms a bouble bond and R_8 is nonexistent; or pharmaceutically acceptable acid addition salts thereof.

2. A process for the preparation of compound of the general formula (Ia) or a pharmaceutically acceptable acid addition salt thereof comprising

reacting a compound of the general formula (2) with a -C(=Y)- group-providing agent in a conventional organic solvent to obtain a

compound of the general formula (3) and successively reacting the compound of the general formula (3) with a compound of the general formula (4) to give the compound of the general formula (5), and reacting the compound of the formula (5) with an alkylating agent or arylating agent in the presence of a base to give the compound of the general formula (Ia).



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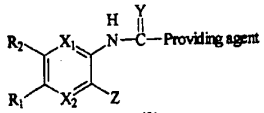

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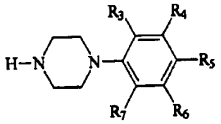

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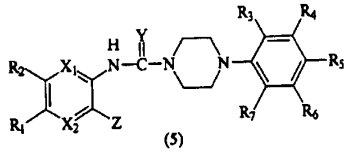

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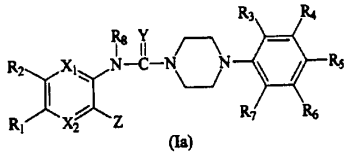


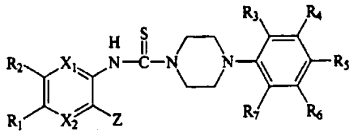
(Ia)

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, X_1, X_2, Y and Z are as defined above, and Lie is a conventional leaving group.

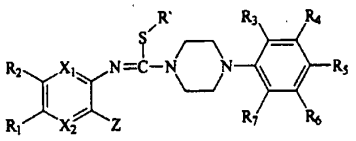
3. A process for the preparation of compound of the general formual (Ib) comprising

reacting a compound of the general formula (II) with an alkylating agent in the presence of a base to give a compound of the general formula (I') and reacting the compound of the formula (I') with a substituted or unsubstitued amine in the presence of a base to give a

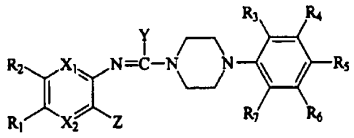
compound of the general formula (Ib).



(II)



(I')



(Ib)

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, X_1, X_2, Y and Z are as defined above, and R' is C_1-C_4 alkyl.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR 00/00164

CLASSIFICATION OF SUBJECT MATTER

IPC[7]: C 07 D 295/108, 295/13, 401/12, 403/12, 213/65, 241/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC[7]: C 07 D 295/00, 401/00, 403/00, 213/00, 241/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

AT, Chemical Abstracts

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Questel: DARC, STN: CA, EPO: WPI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/00402 A1 (SAMJIN) 8 January 1998 (08.01.98) totality.	1-3
X	WO 96/21648 A1 (SAMJIN) 18 July 1996 (18.07.96) totality.	1-3

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
„A" document defining the general state of the art which is not considered to be of particular relevance
„E" earlier application or patent but published on or after the international filing date
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Date of the actual completion of the international search	Date of mailing of the international search report
2 June 2000 (02.06.2000)	28 July 2000 (28.07.2000)
Name and mailing adress of the ISA/AT Austrian Patent Office Kohlmarkt 8-10; A-1014 Vienna Facsimile No. 1/53424/535	Authorized officer Hammer Telephone No. 1/53424/374

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/KR 00/00164

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